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(FILE 'HOME' ENTERED AT 08:16:26 ON 21 DEC 2000)

FILE 'HCAPLUS' ENTERED AT 08:16:35 ON 21 DEC 2000

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L1        43485 S EPITHELIAL OR EPITHELIUM
L2         2231 S IMMORTALIZ?
L3          318 S L1 (L) L2
L4         7008 S SV40
L5           57 S L3 AND L4
L6            3 S METAST? AND L5
L7         3398 S SIMIAN VIRUS 40
L8           31 S L7 AND L3
L9           70 S L5 OR L8
L10           3 S L9 AND METAST?
L11       10754 S ONCOGENE#
L12          30 S L3 AND L11
L13        9239 S IMMUNOSTIM?
L14           1 S L12 AND L13
L15       82042 S B7 OR CYTOKINE#
L16           1 S L15 AND L12
L17           4 S L10 OR L14 OR L16
L18       26597 S RAS OR WT1 OR BCL 2 OR P53MUT OR MYC OR HER OR 2 NEU OR
HPV16
L19       28158 S L18 OR E1A
L20         103 S L19 AND L3
L21           4 S L20 AND (L13 OR L15)
L22       22296 S BONE MARROW
L23           3 S L3 AND L22
L24           6 S L23 OR L21 OR L14
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L24 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:861772 HCAPLUS
TITLE: **Immortalized** human middle ear **epithelial** cell lines
INVENTOR(S): Lim, David J.; Chun, Young-Myoung; Rhim, Johng S.
PATENT ASSIGNEE(S): House Ear Institute, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073419	A1	20001207	WO 2000-US14751	20000526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-136736 19990528

AB Human middle ear epithelial cell lines permanently transformed by human papilloma viruses have been obtained. These cell lines are useful for the study of gene and protein expression in otitis media and the identification of chem. and biol. agents that may be useful in the therapy of human otitis media and other diseases of the ear.

IC ICM C12N005-00
ICS C12N005-02; C12Q001-00

CC 9-11 (Biochemical Methods)
Section cross-reference(s): 1

ST **immortalized** middle ear **epithelial** cell; animal cell line human middle ear **epithelium**

IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(18; **immortalized** human middle ear **epithelial** cell lines)

IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(4; **immortalized** human middle ear **epithelial** cell lines)

IT Animal cell line
(CRL PTA-81; **immortalized** human middle ear **epithelial** cell lines)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(E6, of human papilloma virus, in cell **immortalization**; **immortalized** human middle ear **epithelial** cell lines)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(E7, of human papilloma virus, in cell **immortalization**; **immortalized** human middle ear **epithelial** cell lines)

IT Keratins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(K7; **immortalized** human middle ear **epithelial** cell lines)

IT Porins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(aquaporins, detecting change in expression of; **immortalized** human middle ear **epithelial** cell lines)

IT Receptors
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(bacterial, detecting change in expression of; **immortalized** human middle ear **epithelial** cell lines)

IT **Cytokines**
Growth factors, animal

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(detecting change in expression of and screening; **immortalized** human middle ear **epithelial** cell lines)

IT Immunity
(detecting change in expression of mols. of innate; **immortalized** human middle ear **epithelial** cell lines)

IT Bacteria (Eubacteria)
(detecting change in expression of receptors of; **immortalized** human middle ear **epithelial** cell lines)

IT Lactoferrins
Mucins
Surfactant proteins (pulmonary)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(detecting change in expression of; **immortalized** human middle ear **epithelial** cell lines)

IT Ear
(disease, drug screening for treatment of; **immortalized** human middle ear **epithelial** cell lines)

IT Polynucleotides
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(encoding **immortalizing** gene; **immortalized** human middle ear **epithelial** cell lines)

IT Gene, animal
Proteins, general
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(expression in otitis media; **immortalized** human middle ear **epithelial** cell lines)

IT DNA
RL: BOC (Biological occurrence); BUU (Biological use, unclassified); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(for **human papillomavirus 16** integration into cellular DNA; **immortalized** human middle ear **epithelial** cell lines)

IT Transformation, neoplastic
(**immortalization**; **immortalized** human middle ear **epithelial** cell lines)

IT Animal cell line
Drug screening
Plasmid vectors
Retroviral vectors
Test kits
Virus vectors
(**immortalized** human middle ear **epithelial** cell lines)

IT Desmins
Vimentins
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**immortalized** human middle ear **epithelial** cell lines)

IT Gene, microbial
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**immortalizing; immortalized** human middle ear **epithelial** cell lines)
IT Human papillomavirus
Human papillomavirus 16
Human papillomavirus 18
Human papillomavirus 31
Human papillomavirus 33
Human papillomavirus 35
(in cell **immortalization; immortalized** human middle ear **epithelial** cell lines)
IT Antigens
RL: BOC (Biological occurrence); BUU (Biological use, unclassified); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(large T, SV40, exogenous expression of; **immortalized** human middle ear **epithelial** cell lines)
IT Ear
(middle; **immortalized** human middle ear **epithelial** cell lines)
IT Ear
(otitis, otitis media, gene and protein expression in; **immortalized** human middle ear **epithelial** cell lines)
IT Human adenovirus
Simian virus 40
(polynucleotide for cell **immortalization; immortalized** human middle ear **epithelial** cell lines)
IT RNA formation
(replication, retrovirus vector defective in; **immortalized** human middle ear **epithelial** cell lines)
IT Cell proliferation
(screening agents changing; **immortalized** human middle ear **epithelial** cell lines)
IT Hormones, animal
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening; **immortalized** human middle ear **epithelial** cell lines)
IT 9001-63-2, Lysozyme 103220-14-0, Defensin
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(detecting change in expression of; **immortalized** human middle ear **epithelial** cell lines)
IT 113189-02-9, Factor VIII
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**immortalized** human middle ear **epithelial** cell lines)

L24 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:450863 HCAPLUS
DOCUMENT NUMBER: 131:99526
TITLE: Immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis
INVENTOR(S): Pienta, Kenneth J.

PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5925531	A	19990720	US 1997-956844	19971023

AB The present invention provides immortalized human bone marrow endothelial cells which are useful for the study of tumor metastasis. Primary bone marrow endothelial cells from a 25-yr-old Caucasian man were immortalized with SV40 large T antigen to create the HBME-1 cell line. Karyotyping revealed a heterogeneous karyotype with both diploid and hyper-tetraploid populations of cells. The cells adhere to cancer cells, are easily harvested from tissue culture by trypsinization, and grow well in std. DMEM supplemented with 10% FBS. In particular, the human bone marrow endothelial cell lines provided by the invention provide an in vitro model system for screening compds. for the ability to reduce, prevent, or inhibit the metastasis of cancer cells to bone tissue.

IC ICM G01N033-53
ICS C12N005-00
NCL 435007230
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 13, 63
ST **bone marrow epithelium** cell **immortalization**; cancer cell adhesion **bone marrow epithelium** cell; metastasis **bone marrow epithelium** cell
IT Animal cell line
(HBME-1; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)
IT Intestine, neoplasm
(colon; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)
IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(galactose-binding, galectin, screening compds. for modulating binding of **epithelial** and cancer cells; **immortalized** human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)
IT Transformation, neoplastic
(immortalization; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)
IT **Bone marrow**
Cell adhesion
Disease models
Drug screening
Neoplasm
(immortalized human **bone marrow** endothelial cell

line and their adhesion to cancer cells and uses in treatment of metastasis)

IT Antigens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(large T, treatment with SV40 large T antigen for cell line prepn.; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)

IT Antitumor agents
Neoplasm
(metastasis; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)

IT Mammary gland
Prostate gland
(neoplasm; immortalized human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)

IT RGD peptides
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening compds. for modulating binding of **epithelial** and cancer cells; **immortalized** human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)

IT 99896-85-2
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening compds. for modulating binding of **epithelial** and cancer cells; **immortalized** human **bone marrow** endothelial cell line and their adhesion to cancer cells and uses in treatment of metastasis)

REFERENCE COUNT: 33
REFERENCE(S):
(1) Albelda; FASEB J 1990, V4, P2868 HCAPLUS
(2) Almeida-Porada; J Lab Clin Med 1996, V128(4), P399 HCAPLUS
(3) Bautista; Metabolism 1990, V39, P96 HCAPLUS
(6) Galasko; Clin Orthop 1981, V155, P269 HCAPLUS
(7) Gamble; Proc Nat Acad Sci USA 1985, V82, P8667 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:311285 HCAPLUS
DOCUMENT NUMBER: 130:335018
TITLE: Immortalized, homozygous STAT1-deficient mammalian cell lines and their uses
INVENTOR(S): Levy, David; Palese, Peter; Garcia-Sastre, Adolfo; Durbin, Joan Elizabeth
PATENT ASSIGNEE(S): New York University, USA; Mount Sinai School of Medecine
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9923203	A1	19990514	WO 1998-US23500	19981102
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9913808	A1	19990524	AU 1999-13808	19981102
EP 1034254	A1	20000913	EP 1998-957581	19981102
R: AT, BE, CH, DE, FR, GB, IT, LI				
PRIORITY APPLN. INFO.:			US 1997-962740	19971103
			WO 1998-US23500	19981102

AB The present invention is directed to immortalized STAT1-deficient mammalian cell lines. STAT1 is a signal transducer and activator of transcription that becomes phosphorylated when cells are treated with type I or type II interferons and leads to induction of specific gene expression, resulting in establishment of the antiviral state and the other known biol. responses to interferons, including the inhibition of cell proliferation. Cells which lack this gene product are useful for producing high titers of viral stocks, for producing recombinant viral vectors, for testing samples, esp. clin. samples for the presence of virus and for screening candidate compds. or drugs for anti-viral activity.

IC ICM C12N005-00
ICS C12N007-00

CC 9-11 (Biochemical Methods)
Section cross-reference(s): 1, 10, 13, 15

IT Adenoviridae
Animal cell line
Animal tissue
Animal virus
Body fluid
Bone marrow
Cell (biological)
DNA viruses
Drug screening
Epithelium
Fibroblast
Hematopoietic precursor cell
Hepatitis virus
Herpesviridae
Human parainfluenza virus
Immortalization
Immunoassay
Influenza virus
Kidney
Liver
Mammalian cells
Measles virus
Nucleic acid hybridization
PCR (polymerase chain reaction)
RNA viruses
Respiratory syncytial virus
Retroviridae

Sindbis virus
Transformation (genetic)
Vascular endothelium
Vesicular stomatitis virus
Virus
(**immortalized**, homozygous STAT1-deficient mammalian cell lines and uses)

REFERENCE COUNT: 1
REFERENCE(S): (1) Konobe; US 4071618 A 1978

L24 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:172481 HCAPLUS
DOCUMENT NUMBER: 126:167459
TITLE: **Immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics
INVENTOR(S): Dickmanns, Achim; Fanning, Ellen; Pantel, Klaus; Riethmueller, Gerhard
PATENT ASSIGNEE(S): Micromet Gmbh, Germany; Dickmanns, Achim; Fanning, Ellen; Pantel, Klaus; Riethmueller, Gerhard
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700946	A1	19970109	WO 1996-EP2747	19960624
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2224797	AA	19970109	CA 1996-2224797	19960624
AU 9664153	A1	19970122	AU 1996-64153	19960624
EP 839183	A1	19980506	EP 1996-923904	19960624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507834	T2	19990713	JP 1996-503590	19960624
NO 9706036	A	19980203	NO 1997-6036	19971222
PRIORITY APPLN. INFO.:			EP 1995-109860	19950623
			WO 1996-EP2747	19960624

AB A method for immortalizing epithelial tumor cells with metastatic potential is described by integrating and expressing in the tumor cells an immortalizing oncogene and, optionally, a gene encoding an immuno-stimulatory factor. The invention further relates to antibodies which specifically recognize the epithelial tumor cells of the invention, to processes for the prodn. of said tumor cells as well as pharmaceutical and diagnostic compns. comprising said tumor cells and antibodies, resp. Finally the present invention relates to the use of the epithelial tumor cells and/or antibodies of the invention for the prepn. of tumor vaccines and medicaments for the prophylaxis and/or treatment of cancer and/or the

metastasis of cancer. Immortalization of epithelial tumor cells from patients with prostate cancer, renal cell caner, etc., using SV40 large T antigen was shown.

IC ICM C12N005-10
ICS C07K016-30; A61K039-00; A61K039-395; G01N033-53

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 14

ST **immortalization** human **epithelium** tumor cell **oncogene**

IT **Immunostimulants**
(co-transformation of **epithelial** tumor cells with **oncogene** and; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT Antitumor agents
(development of; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)

IT **Bone marrow**
(**epithelial** tumor cells derived from; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT Genetic elements
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene **E1A** RNA formation factor-responsive element, **immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)

IT Diagnosis
Epithelium
Immortalization
Metastasis (tumor)
(**immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT **WT1** gene (animal)
bcl-2 gene (animal)
ras gene (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)

IT **Human papillomavirus 18**
(**immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)

IT c-erbB2 gene (animal)
c-**myc** gene (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing

oncogene for developing diagnostics)
IT Large T antigen
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(of SV40; **immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)
IT Genes (animal)
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(**p53mut**; **immortalizing** agent; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)
IT Monoclonal antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(to human **epithelial** tumor cells; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)
IT Genes
RL: BAC (Biological activity or effector, except adverse); BUU (Biological
use, unclassified); BIOL (Biological study); USES (Uses)
(transforming; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** and use for developing diagnostics)
IT Vaccines
(tumor; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)
IT **Human papillomavirus**
(type **16**; **immortalizing** agent of; **immortalization** of **epithelial** tumor cell with metastatic potential by introducing **oncogene** for developing diagnostics)

L24 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:118078 HCAPLUS
DOCUMENT NUMBER: 124:137843
TITLE: Transgenic animals and conditionally immortalized cell
lines carrying an immortalizing gene and their uses
INVENTOR(S): Whitehead, Robert H.; Joseph, Joan L.
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600285	A1	19960104	WO 1995-US7255	19950607

W: AU, CA, JP, KR, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9528195 A1 19960119 AU 1995-28195 19950607
PRIORITY APPLN. INFO.: AU 1994-6471 19940624
WO 1995-US7255 19950607

AB Animals bearing an immortalizing gene, e.g. SV40 large T antigen, adenovirus E1A, polyoma virus middle T antigen, together with one or more genes of interest, and cell lines capable of long terms growth in vitro are described. Cell lines derived from F1 Immorto/Min mouse hybrid carry a defective Apc allele and are conditionally immortalized by virtue of an expression of a temp. sensitive SV40 large T antigen gene. These cell lines may further be transfected with other genes of interest such as the Ras oncogene to render them tumorigenic. The establishment and characterization of conditionally immortalized tumorigenic cell lines from the intestine and liver of F1 Immorto/Min mice is demonstrated.

IC ICM C12N015-00
ICS C12N005-00

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 14

IT Animal growth regulators
Enzymes
Hormones
Lymphokines and **Cytokines**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disruption of gene for, in transgenic immortalized animal; transgenic animals and conditionally immortalized cell lines carrying immortalizing gene and their uses)

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**E1A**, expression in in conditionally immortalized cells of; transgenic animals and conditionally immortalized cell lines carrying immortalizing gene and their uses)

IT Gene, animal
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(c-**myc**, transgenic animals and conditionally immortalized cell lines carrying immortalizing gene and their uses)

IT Gene, animal
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(c-**ras**, transgenic animals and conditionally immortalized cell lines carrying immortalizing gene and their uses)

IT Intestine
(colon, **epithelium**, cell lines derived from; transgenic animals and conditionally **immortalized** cell lines carrying **immortalizing** gene and their uses)

IT Lymphokines and **Cytokines**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interleukin 2, in culture of conditionally immortalized cells; transgenic animals and conditionally immortalized cell lines carrying immortalizing gene and their uses)

L24 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1989:513439 HCAPLUS
DOCUMENT NUMBER: 111:113439
TITLE: Loss of leukoregulin up-regulation of natural killer but not lymphokine-activated killer lymphocytotoxicity in **human papillomavirus 16** DNA-**immortalized** cervical **epithelial** cells
AUTHOR(S): Furbert-Harris, Paulette M.; Evans, Charles H.; Woodworth, Craig D.; DiPaolo, Joseph A.
CORPORATE SOURCE: Lab. Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: J. Natl. Cancer Inst. (1989), 81(14), 1080-5
CODEN: JNCIEQ; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sensitivity of human cervical epithelial cells immortalized by transfection with human papillomavirus type 16 (HPV16) DNA, to lysis by natural killer (NK) and lymphokine-activated killer (LAK) lymphocytes was evaluated at progressive stages of transformation. Both early- (10-20 wk) and late- (>30 wk) passage HPV16-immortalized cells were resistant to NK lymphocyte cytotoxicity but sensitive to LAK lymphocyte cytotoxicity at lymphocyte-to-cervical cell ratios ranging from 1:1 to 50:1 in a 4-h 51Cr release assay. Treatment of early-passage HPV16 DNA-immortalized cells with 2.5 U/mL of the NK lymphocytotoxicity-sensitizing lymphokine, leukoregulin, for 1 h induced modest sensitivity to NK cells but markedly up-regulated LAK sensitivity 2-3-fold. At the later passages, leukoregulin up-regulation of sensitivity to NK was lost but remained to LAK lymphocytotoxicity. Similarly, an HPV16-pos. human cervical carcinoma cell line, QGU, was also resistant to NK lymphocytotoxicity and sensitive to LAK lymphocytotoxicity; leukoregulin failed to confer sensitivity to the NK-resistant QGU tumor cells and increased their sensitivity to LAK lymphocytotoxicity 1.5-2-fold. Although the HPV-immortalized cervical cells contg. integrated HPV16 DNA were not tumorigenic, they mimicked the response of established HPV16-pos. cervical carcinoma cells. HPV16-immortalized cervical epithelial cells provide a useful model for the study of cytokine modulation of dysplastic and neoplastic cervical epithelial cell sensitivity to natural lymphocytotoxicity.

CC 15-5 (Immunochemistry)
IT Uterus, neoplasm
(cervix, leukoregulin effect on lymphokine-activated and natural killer lymphocyte killing of human papillomavirus-**immortalized** cervical **epithelial** cells in relation to)
IT Uterus, toxic chemical and physical damage
(cervix, **epithelium**, papillomavirus-**immortalized**, killing of, by lymphokine-activated and natural killer lymphocytes, leukoregulin effect on, of humans)
IT Virus, animal
(human papilloma 16, cervical **epithelial** cells **immortalized** by, lymphokine-activated and natural killer lymphocytes killing of, leukoregulin effect on)
IT Lymphocyte
(killer, lymphokine-activated, human papillomavirus-**immortalized** cervical **epithelial** cells killing by,

leukoregulin effect on)
IT Lymphokines and **Cytokines**
RL: BIOL (Biological study)
(leukoregulin, lymphokine-activated and natural killer lymphocytes killing of human papillomavirus-**immortalized** cervical **epithelial** cells response to)
IT Lymphocyte
(natural killer, papilloma virus 16-**immortalized** cervical **epithelial** cells killing by, leukoregulin effect on)

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=> d his

     (FILE 'WPIDS' ENTERED AT 09:44:22 ON 21 DEC 2000)
                DEL HIS Y
L1          1456 S EPITHERLIAL OR EPITHELIUM
L2           486 S IMMORTALI?
L3           577 S IMMORTAL?
L4            46 S L1 AND L3
L5          1296 S ONCOGENE# OR SV40 OR SIMIAN VIRUS 40
L6            20 S L4 AND L5
L7           175 S L1 AND (TUMOR# OR TUMOUR#)
L8            14 S L7 AND L5
L9            27 S L8 OR L6

=> d .wp 1-27


L9   ANSWER 1 OF 27  WPIDS COPYRIGHT 2000   DERWENT INFORMATION LTD
AN   2000-679539 [66]   WPIDS
DNC  C2000-206683
TI   Low adenosine (A) content antisense oligonucleotides which do not trigger
     adenosine receptors during metabolism, useful e.g. for treating cancers
     and respiratory obstructions.
DC   B04 D16
IN   NYCE, J W
PA   (NYCE-I) NYCE J W; (UYEC-N) UNIV EAST CAROLINA
CYC  85
PI   WO 2000062736 A2 20001026 (200066)* EN
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ TZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
            GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
            MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
            UA UG US UZ VN YU ZW
ADT  WO 2000062736 A2 WO 2000-US8020 20000324
PRAI US 1999-127958   19990406
AB   WO 200062736 A UPAB: 20001219
     NOVELTY - Low adenosine (A) content antisense oligonucleotides (oligo(s))
     and compositions (I) comprising them, are new. In the oligo(s), the A is
     replaced by a 'Universal' or alternative base.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
     following:
          (1) a pharmaceutical composition (I), comprising an
     oligonucleotide(s) (oligo(s)) which is (are) effective for alleviating
     bronchoconstriction and/or lung inflammation, allergy(ies), or surfactant
     depletion or hyposecretion, when administered to a mammal (the oligo
     comprises 0-15% adenosine (A) and is antisense to a target selected from
     the initiation codon, the coding region, the 5'-end and the 3'-end
genomic
     flanking regions, the 5' and 3' intron-exon junctions, and regions within
     2 to 10 nucleotides of the junctions of a gene encoding a target
     polypeptide associated with lung airway dysfunction or anti-sense to the
     polypeptide mRNA), combinations of the oligos and/or mixtures of the
     oligos;
          (2) a cell, carrying the oligo(s) of (1);
          (3) a kit (II), comprising a delivery device, (in a separate
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container(s)) the oligo(s) of (I) and instructions for adding a carrier and for use of the kit;

(4) an in vivo method of delivering an anti-sense oligonucleotide(s) (oligo(s)) to one or more target polynucleotide(s), comprising administering into the respiratory system of a subject one or more oligo(s) that are anti-sense to the polynucleotide(s), in an amount effective to reach and hybridize to the target polynucleotide(s), and reduce the production or availability, or to increase the degradation, of the target mRNA, or to reduce the amount of the target polypeptide present in the lungs; and

(5) an in vivo method (III) of delivering an anti-sense oligonucleotide (oligo) to a target polynucleotide associated with bronchoconstriction and/or lung inflammation, allergy(ies) and/or surfactant hypoproduction, comprising administering to a subject the composition (I), which comprises an amount of the oligo(s) effective to reach and hybridize to the target polynucleotide(s), and reduce or inhibit the polynucleotide(s)' transcription and/or expression and, therefore, alleviating the bronchoconstriction and/or lung inflammation, allergy(ies) and/or surfactant hypoproduction.

ACTIVITY - Respiratory; bronchodilator; antiinflammatory; immunosuppressive; antiasthmatic; analgesic; hypotensive; cytostatic.

MECHANISM OF ACTION - Antisense inhibition of nucleic acid/protein expression.

USE - The oligo(s) may be formulated into compositions (I) and used (III) to down-regulate the expression and or activity of target polypeptides associated with lung/respiratory disorders (especially) and malignancies, such as stimulating and activating peptide factors and transmitters, transcription factors, immunoglobulins and antibodies, antibody receptors, cytokines and chemokines, endogenously produced specific and non-specific enzymes, binding proteins, adhesion molecules and their receptors, cytokine and chemokine receptors, adenosine receptors, bradykinin receptors, central nervous system (CNS) and peripheral nervous and non-nervous system receptors, CNS and peripheral nervous and non-nervous system peptide transmitters, defensins, growth factors, vasoactive peptides and receptors, binding proteins and malignancy associated proteins (specific target polypeptides given in the specification or the TECHNOLOGY FOCUS section of abstract). The oligos may be used in this way to treat disorders including respiratory obstruction (especially pulmonary obstruction and/or bronchoconstriction) and/or lung inflammation, allergy(ies) and/or surfactant hypoproduction which are associated with a disease or condition selected from pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), pain, cystic fibrosis (CF), allergic rhynitis (AR), pulmonary hypertension, emphysema, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, bronchitis, and/or cancer (claimed).

ADVANTAGE - The oligo(s) are free of adenosine (A), or have a low A content, this minimizes triggering of adenosine receptors during metabolism. The oligo(s) may be administered in combination with other therapeutic agents.

Two hyper sensitive monkeys (ascaris sensitive) were challenged with inhaled adenosine with and without pretreatment with an antisense oligo (comprising GATGGAGGGCGGCATGGCGGG). The PC40 adenosine was calculated from

the data as being equivalent to the amount of adenosine in mg that causes a 40% decrease in dynamic compliance in hyper-sensitive airways. The oligo was administered at 10 mg/day for 2 days by inhalation. On the third day, the PC40 adenosine was measured again. The PC40 value prior to the treatment with the oligo was compared to the PC40 adenosine taken after administration of the oligo. The results indicated showed that any sensitivity to adenosine was completely eliminated by administration of the oligo.
Dwg.0/0

L9 ANSWER 2 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-587517 [55] WPIDS
DNC C2000-175293
TI New nucleic acid encoding hemocyanin, useful for gene therapy of **tumors** and for recombinant production of fusion proteins for vaccination.
DC B04 D16
IN ALTENHEIN, B; LIEB, B; MARKL, J; STIEFEL, T
PA (BIOS-N) BIOSYN ARZNEIMITTEL GMBH
CYC 92
PI WO 2000055192 A2 20000921 (200055)* DE 162p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 19911971 A1 20001005 (200057)
ADT WO 2000055192 A2 WO 2000-EP2410 20000317; DE 19911971 A1 DE 1999-19911971 19990317
PRAI DE 1999-19939578 19990820; DE 1999-19911971 19990317
AB WO 200055192 A UPAB: 20001102
NOVELTY - Nucleic acid (I) containing a sequence that encodes hemocyanin (II), a domain of (I) or its fragment with the immunological properties of at least one domain of (II), are new.
DETAILED DESCRIPTION - Nucleic acid (I) is:
(1) any of 67 sequences reproduced (as RNA or DNA);
(2) a sequence that hybridizes with the complementary strand of (i) and encodes a polypeptide (IIa) with the immunological properties of at least one domain of (II);
(3) equivalent within the degeneracy of the genetic code to (i) or (ii) and encodes (IIa);
(4) hydridizes to any of (i)-(iii) and has a complement that encodes (IIa), (v) is at least 60% homologous with (i);
(5) a variant of (i)-(iv) with additions, deletions, insertions or inversions and encodes (IIa), or
(6) a combination of any of (i)-(vi)
INDEPENDENT CLAIMS are also included for the following:
(a) constructs comprising (I);
(b) prokaryotic or eukaryotic host cells containing and expressing the construct of (a);
(c) a method of producing hemocyanin polypeptides by expressing (I) or the construct of (a) in host cells;
(d) hemocyanin polypeptides (III) that include an amino acid sequence

encoded by one or more (I);
(e) recombinant (III) produced by method (c), and its modified forms;
(f) pharmaceutical compositions containing (I) and/or the construct of (a), or (III), plus an additive;
(g) liposomes containing (I), the construct of (a) and/or (III);
(h) antibodies (Ab) produced by immunization with recombinant (III); and
(i) a screening method for identifying **tumor**-specific DNA in a cell.
ACTIVITY - Cytostatic; virucide; antibacterial; antiparasitic; immunomodulatory; antihypertensive.
No suitable biological data is given.
MECHANISM OF ACTION - Vaccine.
USE - (I), and constructs additionally containing antigen-encoding sequences, are useful in gene therapy of **tumors**. Polypeptides encoded by (I) are useful for treating parasitic or viral infections and **tumors**, particularly schistosomiasis and carcinoma (of bladder, **epithelium**, ovary, breast, bronchi or colon-rectum), also hypertension, as vaccines, for treating cocaine misuse and very generally as carriers for pharmaceuticals, e.g. cytostatics. They may also be used to generate antibodies (Ab). Probes based on (I) and Ab are useful for detecting **tumor**-specific DNA in a cell (by detecting specific binding to cellular DNA or proteins), particularly where associated with the types of carcinoma listed above.
ADVANTAGE - Hemocyanins can be produced recombinantly, relatively inexpensively and in adequate amounts, eliminating the need to culture gastropods. When used as a carrier, (II) significantly increases the half-life of the attached pharmaceutical, by inhibiting ultrafiltration in the kidneys.
Dwg.0/11

L9 ANSWER 3 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-423434 [36] WPIDS
CR 2000-423433 [36]
DNN N2000-315925 DNC C2000-128253
TI Novel nucleotide sequence derived from mouse villin gene for targeted expression of transgenes in immature and differentiated epithelial cells of intestine or urogenital tracts.
DC B04 D16 P14
IN JAISSER, F; LOUVARD, D; NIEWOEHNER, J; PINTO, D; ROBINE, S
PA (CNRS) CENT NAT RECH SCI; (CURI-N) INST CURIE
CYC 90
PI WO 2000034493 A2 20000615 (200036)* EN 52p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000019766 A 20000626 (200045)
ADT WO 2000034493 A2 WO 1999-EP9782 19991209; AU 2000019766 A AU 2000-19766 19991209
FDT AU 2000019766 A Based on WO 200034493
PRAI WO 1998-EP8009 19981209
AB WO 200034493 A UPAB: 20000918

NOVELTY - Nucleotide sequence (I) derived from the 5' sequence of the murine villin gene (having a size of 9 kb on an agarose gel) or its fragment, comprising the nucleotide elements having a cis-regulatory activity that promotes the transcription of the murine villin gene, is new.

DETAILED DESCRIPTION - (I) has a fully defined 8995 bp sequence (given in the specification).

INDEPENDENT CLAIMS are also included for the following:

(1) recombinant nucleotide (NT) sequence (II) comprising (I) and another NT sequence capable of tissue specific targeted expression in epithelial intestine cells;

(2) recombinant cell (III) comprising (II);

(3) transgenic animal (IV) expressing (II); and

(4) preparing a transgenic animal comprising:

(i) administration of a transgene into the pronuclei of a fertilized ova;

(ii) enabling the development of the transformed ova

(iii) recovering the transgenic animal (founder) and verifying the presence of the transgene; and

(iv) crossing the founder with a non-transgenic animal.

USE - (I) is useful for targeted expression of transgene in immature and differentiated epithelial cells of the intestine and urogenital tracts

and for establishing **immortal** new cell lines. (II) comprising an **oncogene** is useful for studies relating to carcinogenesis in animal models by expressing the recombinant sequence.

Dwg.0/9

L9 ANSWER 4 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-423433 [36] WPIDS
CR 2000-423434 [36]
DNN N2000-315924 DNC C2000-128252
TI Novel nucleotide sequence derived from mouse villin gene for targeted expression of transgenes in immature and differentiated epithelial cells of intestine or urogenital tracts.
DC B04 D16 P14
IN JAISSER, F; LOUVARD, D; PINTO, D; ROBINE, S
PA (CNRS) CENT NAT RECH SCI; (CURI-N) INST CURIE
CYC 82
PI WO 2000034492 A1 20000615 (200036)* EN 54p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9922692 A 20000626 (200045)
ADT WO 2000034492 A1 WO 1998-EP8009 19981209; AU 9922692 A WO 1998-EP8009 19981209, AU 1999-22692 19981209
FDT AU 9922692 A Based on WO 200034492
PRAI WO 1998-EP8009 19981209
AB WO 200034492 A UPAB: 20000918
NOVELTY - Nucleotide sequence (I) derived from the 5' sequence of the murine villin gene (having a size of 9 kb on an agarose gel) or its fragment, comprising the nucleotide elements having a cis-regulatory activity that promotes the transcription of the murine villin gene, is new.

DETAILED DESCRIPTION - (I) has a fully defined 8995 bp sequence (given in the specification)

INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant nucleotide (NT) sequence (II) comprising (I) and another NT sequence for which a tissue specific targeted expression in epithelial intestine cells is sought;

(2) a recombinant cell (III) comprising (II);

(3) a transgenic animal (IV) expressing (II); and

(4) preparing a transgenic animal comprising:

(i) administration of a transgene into the pronuclei of a fertilized ova;

(ii) enabling the development of the transformed ova;

(iii) recovering transgenic mice (founders) and verifying the presence of the transgene; and

(iv) crossing the founder with non-transgenic mice.

USE - (I) is useful for targeted expression of a transgene in immature and differentiated epithelial cells of the intestine and urogenital tracts and for establishing new **immortal** cell lines. (II) comprising an **oncogene** is useful for studies relating to carcinogenesis in animal models by expressing the recombinant sequence.

DESCRIPTION OF DRAWING(S) - The figure shows the targeted expression of the beta -galactosidase protein using regulatory sequences of the mouse villin gene.

Dwg.7/9

L9 ANSWER 5 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-634001 [54] WPIDS
DNC C1999-185247
TI Human keratinocyte cell line **immortalized** with oncogenic retroviral but not tumorigenic, used for testing, protein production or as artificial skin.
DC B04 D16 D22
IN BAUR, M
PA (NEST) SOC PROD NESTLE SA; (NEST) SOC PROD NESTLE
CYC 70
PI WO 9954435 A2 19991028 (199954)* FR 25p
RW: AT BE CH CY DE DK ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9938135 A 19991108 (200014)
ADT WO 9954435 A2 WO 1999-EP2347 19990407; AU 9938135 A AU 1999-38135 19990407
FDT AU 9938135 A Based on WO 9954435
PRAI EP 1998-201247 19980417
AB WO 9954435 A UPAB: 19991221
NOVELTY - Human keratinocyte cell line (A), **immortalized** by at least one tumorigenic retroviral gene is new.

DETAILED DESCRIPTION - Human keratinocyte cell line (A), **immortalized** by at least one tumorigenic retroviral gene is new and:

(a) is non-tumorigenic;

(b) remains able to differentiate and to express proteins and enzymes

expressed by normal differentiated keratinocytes, even after many passages in tissue culture; and

(c) forms a stratified, polarized **epithelium**, comprising an orthokeratosic stratum corneum, when grown in organotypic culture in serum-free medium without a layer of feeder cells.

INDEPENDENT CLAIMS are also included for the following:

(1) an improved method for producing **immortalized** keratinocytes from human skin cells; and

(2) an artificial skin comprising (A).

USE - (A) are used:

(i) for performing immunological, pharmacological or toxicological tests (typical of many applications are studies of barrier functions, metabolism, effects of light and sensitizing agents; selection of anticancer agents and agents for treating other skin diseases; identification of mutagens etc.);

(ii) for expression of heterologous genes (for producing proteins or nucleic acids) and

(iii) as artificial skin (particularly when combined with collagen, fibroblasts and melanocytes).

ADVANTAGE - (A) retain all the differentiation markers of normal keratinocytes and form ortho-keratosic (rather than para-keratosic) **epithelium** (i.e. the stratum corneum does not include nucleated cells), so are especially suitable wherever highly differentiated skin cells are required.

Dwg.0/2

L9 ANSWER 6 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-532005 [45] WPIDS
DNC C1998-159717
TI New nucleic acid encoding NOEY2 **tumour** suppressor from ovarian **epithelium** - useful for, e.g. treatment, diagnosis and prognosis of cancer, particularly cancer of ovary and breast.
DC B04 D16
IN BAST, R C; XU, F; YU, Y
PA (TEXA) UNIV TEXAS SYSTEM
CYC 82
PI WO 9842830 A2 19981001 (199845)* EN 181p
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9865805 A 19981020 (199909)
EP 988376 A2 20000329 (200020) EN
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 9842830 A2 WO 1998-US5723 19980320; AU 9865805 A AU 1998-65805 19980320; EP 988376 A2 EP 1998-911977 19980320, WO 1998-US5723 19980320
FDT AU 9865805 A Based on WO 9842830; EP 988376 A2 Based on WO 9842830
PRAI US 1998-71263 19980113; US 1997-41580 19970321
AB WO 9842830 A UPAB: 19981111
New nucleic acid (I) comprises a NOEY2 gene encoding a 228 amino acid (aa)

(S1) protein (P1) (sequence is given in the specification). Also new are: (A) host cells and viruses that contain (I); (B) antibody (Ab) specific

for a polypeptide comprising (S1); (C) transgenic animals having a transgene encoding (P1) in the genome; (D) method for selecting NOEY2 polypeptide mutants with increased **tumour** suppressor activity, and (E) identifying **tumour** suppressor genes or **oncogenes** in a two-hybrid system using a NOEY2 effector domain/DNA binding domain fusion as one reactant.

USE - (P1) is a **tumour** suppressor, isolatable from ovarian epithelial cells. (I) is used to express recombinant (P1), to treat cancer (particularly of breast and ovary, but more generally to suppress tumorigenesis in any cell type); in gene therapy of cancer and to prepare transgenic animals. Immunodominant epitopes of (P1) are useful for vaccination. Ab, particularly labelled, are used for immunodetection of (P1), for diagnosis, prognosis and staging of cancers, and also therapeutically, optionally coupled to a drug or toxin, and optionally used in conjunction with gene therapy, chemotherapy or radiation treatment. Fragments of (I) are also used, as probes and primers in usual hybridisation, amplification and sequencing methods, for diagnosis, including detection of mutations, or as antisense molecules or ribozymes for reducing/eliminating NOEY2 activity. (I) and (2) can also be used to screen for antitumour agents that stimulate NOEY2, overcome lack of this protein or block expression of mutant NOEY2. Transgenic animals are useful as models of cancer. (I) and (P1) are administered by injection, nasally, vaginally and topically. When (I) is administered in a vector, the dose is typically 10000-1012 infectious particles, or cells (particularly from bone marrow) are transfected in vitro for subsequent return to the patient.

Dwg.4A/8

L9 ANSWER 7 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-530876 [45] WPIDS
DNC C1998-159213
TI **Immortalised** intestinal epithelial cell line - useful as an in vitro model of drug absorption through the gut.
DC B04 D16
IN PAUL, E C A; QUARONI, A
PA (CORR) CORNELL RES FOUND INC
CYC 1
PI US 5811281 A 19980922 (199845)* 15p
ADT US 5811281 A CIP of US 1993-89847 19930712, US 1994-342434 19941118
PRAI US 1994-342434 19941118; US 1993-89847 19930712
AB US 5811281 A UPAB: 19981111

A new intestinal epithelial cell line cultured in vivo consists of conditionally **immortalised** intestinal epithelial cells containing heterologous DNA comprising a temperature-sensitive mutant **oncogene**. The **oncogene** is one of adenovirus Ela, **SV40** large T antigen, polyomavirus large T antigen, papilomavirus E7, myc, fos, or p53. At a permissive temperature, expression of the **oncogene** results in a functional protein, effecting the cell line, and a shift to a nonpermissive temperature results in an absence of the functional protein and cessation of cell proliferation, and at least the differentiated intestinal epithelial cell phenotype characterised by expression of brush border enzymes sucrase isomaltase and aminopeptidase N

and dipeptidyl IV, expression of keratin markers keratin 8 and keratin 21,
and expression of peripheral membrane ZO-1.
USE - The cell line can be used in research to evaluate characteristics of absorptive villi. By establishing a cell line so its proliferation can be adjusted, the cell line can be maintained for extended periods of time. This is especially useful as most pharmaceutical drugs are administered orally, and data is required on rates of absorption, metabolism and intercellular interactions. Conventional methods of testing rely on in vivo animal models and results are difficult to interpret because of lack of accessibility to the intestine, interactions with other systems, costs of maintaining animals etc.
ADVANTAGE - **Oncogene** control of the cell line enables it to be maintained in culture for extended periods of time. Previous in vitro cultures of intestinal cells can only be maintained for 2-3 hours, and additionally, any cultures that have been maintained, cannot be differentiated into the absorptive villi type.
Dwg.0/7

L9 ANSWER 8 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-436534 [37] WPIDS
CR 1997-051178 [05]
DNC C1998-132632
TI Human corneal epithelial cell line - transfected with viral **SV40** genes to give the cell line an extended life-span.
DC B04 D16
IN KAHN, C R; RHIM, J
PA (GILL) GILLETTE CO
CYC 1
PI US 5786201 A 19980728 (199837)* 21p
ADT US 5786201 A Cont of US 1992-983226 19921130, Cont of US 1994-253585 19940603, US 1995-474399 19950607
PRAI US 1992-983226 19921130; US 1994-253585 19940603; US 1995-474399 19950607
AB US 5786201 A UPAB: 19980916
An **immortalised** human corneal epithelial cell line contains actively expressing **SV40** genes, where:
(a) the cell line maintains the phenotypic properties of human corneal epithelial cells in vivo; or
(b) the cell line when cultured upon collagen membranes, achieve 3-5 cell layers of stratification, and retard flow of Na-fluorescin across the air-liquid interface by 80-95%.
USE - The cell line is useful as an in vitro model of the human ocular surface. This can then be used to test foods, drugs, cosmetics etc, to see their physiological effect on biochemical and tissue specific mechanisms. The transfection of the cells with viral genomic derivatives allow **immortalisation** of the cell line.
ADVANTAGE - An in vitro model allows damaging experiments to be carried out without harming prior ocular models e.g. rabbits and mice. It also allows specific reactions to be seen as they would occur in humans as animal models may react differently to human models, to different stimuli.

Also prior cell lines had finite life spans.
Dwg.0/12

L9 ANSWER 9 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-286977 [25] WPIDS
DNC C1998-089008
TI Antisense oligonucleotides that down regulate the erbB-2 **oncogene** - useful to inhibit ERBB2 tyrosine kinase receptor expression in cancer cells to treat epithelial cell, breast, ovarian, lung or colon cancer.
DC B04 D16
IN INGLEHART, J D; MARKS, J R; VAUGHN, J P
PA (UYDU-N) UNIV DUKE
CYC 21
PI WO 9820168 A1 19980514 (199825)* EN 31p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9852594 A 19980529 (199841)
US 5910583 A 19990608 (199930)
ADT WO 9820168 A1 WO 1997-US20910 19971103; AU 9852594 A AU 1998-52594 19971103; US 5910583 A US 1996-740821 19961104
FDT AU 9852594 A Based on WO 9820168
PRAI US 1996-740821 19961104
AB WO 9820168 A UPAB: 19980624
Antisense oligonucleotides that down regulate the erbB-2 **oncogene** with sequence (I) ('US-3') or (II) ('UT-1') are new. GGTGCTCACTGCGGC (I) TGCGGCTCCGGCCCC (II)
USE - The oligonucleotides are useful as antisense oligonucleotides for inhibiting the expression of the ERBB2 tyrosine kinase receptor in a cell, in vitro or in vivo (claimed); such cells may be e.g. epithelial or **tumour** cells, especially breast cancer, ovarian cancer, lung cancer and colon cancer cells (claimed). The oligonucleotides are useful in vivo to treat cancer (especially epithelial cell, breast, ovarian, lung or colon cancer) in a human or other animal, especially when the cancer is characterised by cells that overexpress the ERBB2 tyrosine kinase receptor and the oligonucleotides are administered intravenously (claimed). In vitro, they may be used in a prior art process to identify compounds that inhibit the overexpression of the ERBB2 tyrosine kinase receptor. The oligonucleotides can also be included in pharmaceutical compositions with an acceptable carrier (claimed) e.g. for therapeutic administration. The antisense oligonucleotides are targeted to the erbB-2 **oncogene** since this is overproduced in a high proportion of breast and other epithelial cancers, but shows low expression in most normal adult tissues, making it an attractive therapeutic target. The oligonucleotides may also be labelled with a suitable detectable group (e.g. a radioisotope) and used as hybridisation probes to detect the ERBB2 gene, or the molecular weights of the oligonucleotides determined and the oligonucleotides used as molecular weight markers.
Dwg.0/5

L9 ANSWER 10 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-535824 [49] WPIDS
DNC C1997-171380

TI **Immortalised** endothelial or epithelial cells from mammalian retina contain viral **oncogene** - are used for preventing loss of photoreceptors, as carriers for therapeutic genes and as models for studying the retinal-blood barrier.
DC B04 D16
IN ADAMSON, P; GREENWOOD, J; LUND, R
PA (NEUR-N) NEUROTECH SA; (UYBR-N) UNIV BROWN RES FOUND
CYC 23
PI WO 9740139 A1 19971030 (199749)* FR 52p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP NZ US
FR 2747690 A1 19971024 (199750) 20p
AU 9727041 A 19971112 (199811)
EP 833895 A1 19980408 (199818) FR
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
NZ 329360 A 19990528 (199927)
JP 11508142 W 19990721 (199939) 48p
US 6090624 A 20000718 (200037)
AU 725173 B 20001005 (200054)
ADT WO 9740139 A1 WO 1997-FR709 19970418; FR 2747690 A1 FR 1996-4964 19960419;
AU 9727041 A AU 1997-27041 19970418; EP 833895 A1 EP 1997-920791 19970418,
WO 1997-FR709 19970418; NZ 329360 A NZ 1997-329360 19970418, WO 1997-FR709
19970418; JP 11508142 W JP 1997-537783 19970418, WO 1997-FR709 19970418;
US 6090624 A CIP of US 1998-973553 19980122, US 1998-182516 19981030; AU
725173 B AU 1997-27041 19970418
FDT AU 9727041 A Based on WO 9740139; EP 833895 A1 Based on WO 9740139; NZ
329360 A Based on WO 9740139; JP 11508142 W Based on WO 9740139; AU 725173
B Previous Publ. AU 9727041, Based on WO 9740139
PRAI FR 1996-4964 19960419
AB WO 9740139 A UPAB: 19971211
Immortalised cell lines, derived from primary cultures of endothelial or epithelial mammalian retinal cells, contain a nucleic acid fragment (I) containing at least an **immortalising** fragment (A) of a heat-sensitive viral **oncogene**, optionally also a selection gene (II). The cells retain the morphological characteristics and at least the surface-antigen expressing characteristics of the corresponding primary cultures. Also new are vector cells comprising these cells and a vector that contains a sequence encoding a polypeptide, protein or viral vector (collectively (B)), optionally also selection and marker genes. These cells can integrate in vivo into the retina (particularly the subretinal space) to prevent loss of photoreceptors and to express (B).

The cells are derived from (a) endothelial cells or (b) pigmentary epithelial cells able to integrate into retinal tissue. (I) contains a fragment of the large T antigen of **simian virus 40**. Specified cell lines are IO/JG2/1 (endothelial) and IO/LD7/4 (epithelial), deposited as CNCM I-1695 and -1694, respectively.

USE - The cell lines are models for studying and identifying biological/cellular systems in the blood-retinal barrier. Transfected epithelial cells are also used (by implantation in the retina) to treat primary or secondary ophthalmological and neurological disorders, e.g. retinal degeneration.

ADVANTAGE - The cell lines are stable (preferably for at least 50

passages) and have most of the characteristics of differentiated cells. They are pure and homogeneous, and can be produced in sufficient quantity to serve as transplant material. The vector cells are very well tolerated and express (B) over a long period.
Dwg.12/17

L9 ANSWER 11 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-350246 [32] WPIDS
DNC C1997-113061
TI **Immortalised** human lens epithelial cell line - useful for research in cataract formation and for assaying lens inhibitory drugs.
DC B04 D16
IN ANDLEY, U P; FLEMING, T P
PA (UNIW) UNIV WASHINGTON
CYC 1
PI US 5643782 A 19970701 (199732)* 11p
ADT US 5643782 A US 1993-110726 19930823
PRAI US 1993-110726 19930823
AB US 5643782 A UPAB: 19970806
Immortalised human lens epithelial cell line that produces a beta -crystallin comprises human lens epithelial cell line ATCC CRL 11421 infected with hybrid adenovirus Ad12-**SV40**. Also claimed are: (1) a human lens epithelial cell culture obtained by infecting human lens epithelial cells having all the identifying characteristics of cell line ATCC CRL 11421, and (2) a method of producing the above cell line.
USE - The **immortalised** human lens epithelial cell line is used for studying human lens physiology, for investigating the role of lens **epithelium** in cataract formation and for determining the effect of drugs on cataract formation.
ADVANTAGE - The **immortalised** human lens epithelial cell line retains the ability to synthesise beta and gamma -crystallins, indicating that **immortalising** event has not altered the cells normal differentiating function.
Dwg.0/8

L9 ANSWER 12 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-087373 [08] WPIDS
DNN N1997-071901 DNC C1997-028474
TI New **immortalised** epithelial **tumour** cells - having **immortalising oncogene** introduced into genome(s) or another replicating genetic element.
DC B04 D16 S03
IN DICKMANNS, A; FANNING, E; PANTEL, K; RIETHMULLER, G; RIETHMUELLER, G
PA (MICR-N) MICROMET GMBH
CYC 72
PI WO 9700946 A1 19970109 (199708)* EN 47p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9664153 A 19970122 (199719)
NO 9706036 A 19980203 (199816)
EP 839183 A1 19980506 (199822) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11507834 W 19990713 (199938) 44p
ADT WO 9700946 A1 WO 1996-EP2747 19960624; AU 9664153 A AU 1996-64153

19960624; NO 9706036 A WO 1996-EP2747 19960624, NO 1997-6036 19971222; EP 839183 A1 EP 1996-923904 19960624, WO 1996-EP2747 19960624; JP 11507834 W WO 1996-EP2747 19960624, JP 1997-503590 19960624
FDT AU 9664153 A Based on WO 9700946; EP 839183 A1 Based on WO 9700946; JP 11507834 W Based on WO 9700946
PRAI EP 1995-109860 19950623
AB WO 9700946 A UPAB: 19970220
Epithelial **tumour** cell (ETC) with metastatic potential comprises integrated in its genome or another replicative genetic element an externally introduced **immortalising oncogene** which is expressed in the cell.

Also claimed is an antibody or fragment or deriv. of the antibody or fragment which specifically recognises a **tumour** cell such as ETC.

USE - The ETC or antibody can be used for the prophylaxis and/or treatment of cancer and/or cancer metastasis. They can also be used for the prepn. of **tumour** vaccines. They can also be used in diagnostic compsns. The ETC can also be used for the ex vivo stimulation of a patient's immune cells. The cells are used in pharmaceutical and diagnostic compsn. (all claimed).

ADVANTAGE - The ETCs provide for the specific and unlimited expansion of **tumour** cells of epithelial origin with metastatic potential.
Dwg.0/5

L9 ANSWER 13 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-051178 [05] WPIDS
CR 1998-436534 [37]
DNC C1997-016864
TI Prodn. of **immortalised** human corneal epithelial cell line - by culturing cells in serum-free medium, transforming with vector contg. **SV40** early region genes and recovering continuously growing cells.
DC B04 D16
IN KAHN, C R; RHIM, J
PA (GILL) GILLETTE CO
CYC 1
PI US 5585265 A 19961217 (199705)* 23p
ADT US 5585265 A Cont of US 1992-983226 19921130, US 1994-253585 19940603
PRAI US 1992-983226 19921130; US 1994-253585 19940603
AB US 5585265 A UPAB: 19980916
Prodn. of an **immortalised** human corneal epithelial cell line comprises: (a) culturing human corneal epithelial cells in a serum-free medium; (b) transforming the cells with a vector contg. **SV40** early region genes so that the cells become continuously growing; and (c) recovering continuously growing cells, which when cultured on collagen membranes, achieve 3-5 cell layers of stratification and retard the flow of sodium fluorescein across the air-liq. interface by 80-95%. Also claimed is the above cell line.

USE - The method is used for determining the effect of chemicals or drugs on the eye (claimed). The cell lines may be used as e.g. model systems to experiment on wound healing of the human cornea, host-parasite interactions, radiation biology, genetic engineering and as a model system for viral infection and diseases of the eye.
Dwg.0/12

L9 ANSWER 14 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1996-040231 [04] WPIDS
DNC C1996-013602
TI Transgenic non-human animal expressing progressive epithelial neoplasia -
useful as an improved model for cervico-vaginal neoplasia.
DC B04 D16
IN ARBEIT, J M; HANAHAN, D
PA (REGC) UNIV CALIFORNIA
CYC 64
PI WO 9533826 A1 19951214 (199604)* EN 41p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE
KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE
SG SI SK TJ TM TT UA UZ VN
AU 9528224 A 19960104 (199613)
US 5709844 A 19980120 (199810) 14p
ADT WO 9533826 A1 WO 1995-US7350 19950609; AU 9528224 A AU 1995-28224 19950609; US 5709844 A CIP of US 1994-257339 19940609, US 1995-484997 19950607
FDT AU 9528224 A Based on WO 9533826
PRAI US 1995-484997 19950607; US 1994-257339 19940609
AB WO 9533826 A UPAB: 19960129
A novel transgenic, non-human animal expressing progressive epithelial neoplasia comprises a human papillomavirus (HPV) **oncogene** operably linked to a promoter which directs its expression in a transient amplifying cell in the animal.
USE - The transgenic, non-human animal is an improved model for progressive epithelial neoplasias, pref. cervico-vaginal neoplasia. It can be used to test cpds. for their ability to inhibit epithelial neoplasia. The animals are useful for developing new therapeutic agents. The animals can also be used to screen and identify potential carcinogens directly.
ADVANTAGE - The animals have multiple squamous epithelial sites affected by expression of the transgene, and discrete, multistep neoplastic progression of the epidermis. These features can be used to assess the systemic co-carcinogenicity of multiple environmental agents, and the ability of agents to abrogate this systemic initiation. The progression is similar to clinical HPV disease and epithelial carcinogenesis, and so can be used to investigate topical co-carcinogenesis and/or chemoprevention, as they interact with a cancer-associated DNA **tumour** virus.
Dwg.0/0

L9 ANSWER 15 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-040228 [04] WPIDS
DNC C1996-013599
TI Transgenic, non-human animal expressing progressive epithelial neoplasia - is an improved model for gynaecological malignancy.
DC B04 D16
IN ARBEIT, J M; HANAHAN, D; HOWLEY, P M
PA (REGC) UNIV CALIFORNIA; (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 63
PI WO 9533820 A1 19951214 (199604)* EN 51p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE
KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE
SG SI SK TJ TT UA UG UZ VN

AU 9526954 A 19960104 (199613)
US 5698764 A 19971216 (199805) 14p
ADT WO 9533820 A1 WO 1995-US6981 19950602; AU 9526954 A AU 1995-26954 19950602; US 5698764 A US 1994-258846 19940609
FDT AU 9526954 A Based on WO 9533820
PRAI US 1994-258846 19940609
AB WO 9533820 A UPAB: 19960129
Transgenic, non-human animal expressing progressive epithelial neoplasia comprises a human papillomavirus (HPV) **oncogene** operably linked to a promoter which directs its expression in a transient amplifying cell in the animal. Also claimed are: (1) a recombinant DNA construct comprising an expression cassette including an HPV **oncogene** as above; and (2) a method for testing a cpd. for its ability to inhibit epithelial neoplasia induced by an HPV **oncogene** by: (a) providing the transgenic, non-human animal; (b) administering the compsn. to the animal, and (c) detecting epithelial neoplasia in the animal.
USE - The transgenic, non-human animal is an improved model for progressive epithelial neoplasias, pref. gynaecological malignancy. It can be used to test cpds. for their ability to inhibit epithelial neoplasia. The animals have multiple squamous epithelial sites affected by expression of the transgene, and discrete, multistep neoplastic progression of the epidermis. These features can be used to assess the systemic co-carcinogenicity of multiple environmental agents, and the ability of agents to abrogate this systemic initiation. The progression is similar to clinical HPV disease and epithelial carcinogenesis, and so can be used to investigate topical co-carcinogenesis and/or chemoprevention, as they interact with a cancer-associated DNA **tumour** virus. The animals are also useful for developing new therapeutic agents. The animals can also be used to screen and identify potential carcinogens directly, and to investigate the effect of prolonged exposure to oestrogen or related cpds.
Dwg.0/0

L9 ANSWER 16 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-403863 [51] WPIDS
DNC C1995-173442
TI **Immortalised** human prostatic cell lines - obtd. by **immortalising** prostatic epithelial or fibroblast cells with a hybrid adenovirus-simian virus.
DC B04 D16
IN RHIM, J S; WEBBER, M M
PA (UNMS) UNIV MICHIGAN STATE; (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 18
PI WO 9529994 A1 19951109 (199551)* EN 57p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA
US 5610043 A 19970311 (199716) 19p
US 5716830 A 19980210 (199813) 18p
US 5814452 A 19980929 (199846)
CA 2187099 C 19991109 (200013) EN
ADT WO 9529994 A1 WO 1995-US5389 19950424; US 5610043 A US 1994-234981 19940428; US 5716830 A Div ex US 1994-234981 19940428, US 1997-805596 19970225; US 5814452 A Div ex US 1994-234981 19940428, US 1997-806551

19970225; CA 2187099 C CA 1995-2187099 19950424, WO 1995-US5389 19950424
FDT US 5716830 A Div ex US 5610043; US 5814452 A Div ex US 5610043; CA 2187099
C Based on WO 9529994
PRAI US 1994-234981 19940428; US 1997-805596 19970225; US 1997-806551 19970225
AB WO 9529994 A UPAB: 19951221
Immortalised adult human normal prostatic epithelial or fibroblast cell derived cell line (A) (ATCC VR-239) is new, which is free of other cell lines and contains DNA of adenovirus (AdV) and simian virus (SV) as a hybrid virus, the cell line having the identifying characteristics of the prostatic epithelial or fibroblast cell without the hybrid virus in addition to being **immortalised** by the hybrid virus.

USE - The cell lines can be used to screen carcinogenic chemotherapeutic, chemo-preventive, anti-invasive, anti-metastatic or anti-angiogenic agents. They can also be used to conduct studies on cellular senescence and acquisition of **immortality**, on the mechanisms involved in the loss of **tumour** suppressor gene activity and the consequences of this loss resulting in cancer (claimed).

ADVANTAGE - The **immortalised** cells express many of the characteristics of normal differentiated prostatic cells and so provide useful models. The cell lines are capable of growth in serum-free medium.
Dwg.0/6

L9 ANSWER 17 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-350775 [45] WPIDS
CR 1993-235124 [29]
DNC C1995-153681
TI **Immortalised** ruminant mammary epithelial cell lines - prepd. from goat or sheep cells, having normal physiological responses of such epithelial cells.
DC B04 C06 D16
IN TURNER, J D
PA (UYMC-N) UNIV MCGILL
CYC 1
PI US 5455164 A 19951003 (199545)* 12p
ADT US 5455164 A CIP of US 1989-431294 19891103, US 1993-56028 19930430
FDT US 5455164 A CIP of US 5227301
PRAI US 1993-56028 19930430; US 1989-431294 19891103
AB US 5455164 A UPAB: 19951114
Immortalised ruminant mammary epithelial cell (MEC) line is claimed which is prepd. by the transfection of primary ruminant MECs with the **SV40** large T antigen gene, where the MECs are selected from goat and sheep cells, the cell line having normal physiological responses such that, under hormonal stimulation, milk constituents comprising alpha- and beta-casein and lactose are produced.

USE - The cell lines provide an in vitro system to study lactation, for screening DNA constructs prior to gene transfer or for expressing foreign genes. They can be used for testing the suitability of a foreign DNA construct prior to making a transgenic ruminant animal for prodn. of e.g. human neuropeptide Y, yeast peroxisomal catalase, flounder antifreeze protein, human ferritin, human tissue plasminogen activator, beta-galactosidase, insulin-like growth factor, large T antigen,

aminoglycoside phosphotransferase or hygromycin B phosphotransferase (claimed). They can also be used for the prodn. of alpha- and beta-casein and lactose (claimed).

ADVANTAGE - The cell lines are **immortalised** but not transformed and hence behave in a normal physiological way except for their **immortal** property.

Dwg.0/3

L9 ANSWER 18 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-303015 [37] WPIDS
CR 1989-263494 [36]; 1989-339692 [46]; 1990-051540 [07]; 1996-308740 [31]
DNC C1994-138215
TI New human liver epithelial cell lines - obtd. by infection of liver cells with a retroviral vector contg. the **SV40** large T antigen gene.
DC B04 D16
IN COLE, K H; HARRIS, C C; LECHNER, J F; REDDEL, R
PA (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 21
PI WO 9420607 A1 19940915 (199437)* 48p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9463516 A 19940926 (199503)
EP 687294 A1 19951220 (199604) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5665589 A 19970909 (199742) 16p
US 5759765 A 19980602 (199829)
ADT WO 9420607 A1 WO 1994-US1910 19940303; AU 9463516 A AU 1994-63516 19940303; EP 687294 A1 EP 1994-910730 19940303, WO 1994-US1910 19940303; US 5665589 A CIP of US 1988-284331 19881214, CIP of US 1988-284368 19881214, Cont of US 1989-377967 19890711, CIP of US 1992-879165 19920501, US 1993-25336 19930303; US 5759765 A CIP of US 1988-284331 19881214, CIP of US 1988-284368 19881214, Cont of US 1989-377967 19890711, CIP of US 1992-879165 19920501, Div ex US 1993-25336 19930303, US 1995-458878 19950602
FDT AU 9463516 A Based on WO 9420607; EP 687294 A1 Based on WO 9420607; US 5665589 A CIP of US 5529920; US 5759765 A CIP of US 5529920, Div ex US 5665589
PRAI US 1993-25336 19930303; US 1988-284331 19881214; US 1988-284368 19881214; US 1989-377967 19890711; US 1992-879165 19920501; US 1995-458878 19950602
AB WO 9420607 A UPAB: 19971113
Cells comprising a cell line derived from normal adult human liver tissue are new and have the following characteristics: (a) demonstrate an indefinite life span in vitro, (b) metabolically activate precursor cpds. to DNA-adduct forming cpds. and (c) demonstrate a pattern of gene expression similar to that of normal adult human hepatocyte cells.

USE/ADVANTAGE - The cell lines provide a reproducible source of cells for long-term studies of human carcinogenisis and toxicology. They can be used for evaluating the genotoxicity of a cpd. and for screening a cpd. for potential carcinogenicity (claimed). They can also be used to screen and study therapeutic cpds. The cell lines overcome the deficiencies of previous cell lines with regard to limitation of lifespan or non-human origin.

In an example, a recombinant retrovirus carrying the TAg gene of

SV40 was constructed by insertion of a BglI-HpaI fragment of **SV40** DNA into the BauHI site of the pZipNeoSVX vector. Infections recombinant virus particles were made by transfecting the packaging cell line PA317 with the vector. A pool of virus from the transfected PA317 cells was used to infect primary liver tissue cultures. Infection with the recombinant virus caused the liver cells to undergo rapid division. The THLE-2 cell line was deposited as ATCC CRL 10149 and the THLE-3 cell line was deposited as ATCC CRL 11233.
Dwg.0/5

L9 ANSWER 19 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1993-235124 [29] WPIDS
CR 1995-350775 [45]
DNC C1993-104818
TI An **immortalised** bovine mammary epithelial cell line - prepd. by transfection of prim. bovine mammary epithelial cells with **SV40** large -antigen, used for indefinitely expressing foreign genes.
DC B04 C06 D16
IN HUYNH, H; TURNER, J D
PA (UYMC-N) UNIV MCGILL INST ADVANCEMENT LEARNING
CYC 1
PI US 5227301 A 19930713 (199329)* 7p
ADT US 5227301 A US 1989-431294 19891103
PRAI US 1989-431294 19891103
AB US 5227301 A UPAB: 19951122
Immortalised bovine mammary epithelial cell line (I) prepd. by the transfection of primary bovine mammary epihelial cells with **SV40** large T antigen, is new.
(I) has normal physiological responses so that, under hormonal stimulation it produces milk constituents comprising alpha- and beta-casein and lactose.
Also claimed are: (A) a method of stimulating the prodn. of certain milk proteins by bovine mammary epihelial cells in vitro comprising (a) incubating (I) in a culture medium; (b) adding to the culture medium at least 1 lactation hormones to stimulate prodn. of certain milk proteins by the cell line; and (c) measuring the amt. of alpha- and beta-casein and lactose produced and secreted in the culture medium; and (B) a method of in vitro screening for foreign gene expession in bovines comprises, (a) providing (I); (b) transfecting the cells of (a) with a foreign DNA construct comprising a bovine casein promoter and a foreign gene, where the mammary gland is the target organ for the foreign gene expression, and
(c) assaying the transfected cells of step (b) for the foreign gene expression, thereby determining the suitability of foreign DNA construct prior to making or transgenic bovine.
USE/ADVANTAGE - (I) ATCC number CRL 10274, can be used in a method for indefinitely expressing foreign genes. It also provides a method of studying in vitro lactation due to its normal physiological responses
Dwg.0/1
Dwg.0/1

L9 ANSWER 20 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-151345 [19] WPIDS
TI Non-tumoricidal human cell line - derived from bronchial epithelial or mesogenic cells and grows without senescence in serum-free culture.

DC B04 D16 S03
IN BRASH, D; GERWIN, B I; HARRIS, C C; LECHNER, J F; REDDEL, R R; RHIM, J S; SO, R T; YANG, K
PA (USDC) US DEPT OF COMMERCE
CYC 1
PI CA 1298220 C 19920331 (199219)* 19p
ADT CA 1298220 C CA 1988-581739 19881031
PRAI CA 1988-581739 19881031
AB CA 1298220 C UPAB: 19931006
The non-tumorigenic, human bronchial epithelial or mesothelial cell line (I) or derivative grows without senescence when cultured in vitro in growth medium and has the identifying characteristics of ATCC CRL 9608, 9609, 9442, 9443, 0444, 9482 or 9483.

Also new are: (1) a kit for screening carcinogenic or chemotherapeutic agents comprising a container contg. (I); (2) a method for testing carcinogenicity of an agent comprising culturing (I) with said agent and looking for formation of abnormal cellular mass; and (3) a method for testing antineoplastic activity of an agent comprising adhering (I) with said agent and determining whether growth is inhibited.

USE/ADVANTAGE - (I) is a suitable recipient for transfection of **oncogenes** and can be used to test the cytotoxicity potential of chemical and physical agents, the growth inhibition capability of biological agents and the squamous differentiating potential of chemical and biological agents. It proliferates indefinitely in serum-free medium and contains no **oncogene** found in naturally occurring **tumours**.
0/0

L9 ANSWER 21 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1991-368903 [50] WPIDS
CR 1988-036306 [05]; 1988-147442 [21]; 1989-263488 [36]; 1993-351737 [44]; 1995-035935 [05]
DNC C1991-158969
TI **Immortalised** human cell lines - comprising tumorigenic and non-tumorigenic cell lines of bronchial and mesothelial epithelial cell origin.
DC B04 D16
IN AMSTAD, P; BRASH, D E; GERWIN, B I; HARRIS, C C; KE, Y; LECHNER, J F; REDDEL, R R; RHIM, J S; SU, R T; BRASH, D; REDDELL, R R; RHIM, J; SU, R; YANG, K
PA (USDC) US DEPT OF COMMERCE; (USSH) US DEPT HEALTH & HUMAN SERVICES; (USSH) US DEPT HEALTH & HUMAN SERVICE
CYC 19
PI US 7636712 A 19911112 (199150)*
WO 9212258 A1 19920723 (199232) EN 24p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA JP
AU 9212377 A 19920817 (199245)
EP 567572 A1 19931103 (199344) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06502995 W 19940407 (199419) 10p
US 5443954 A 19950822 (199539) 7p
ADT US 7636712 A US 1991-636712 19910102; WO 9212258 A1 WO 1992-US15 19920102;

AU 9212377 A AU 1992-12377 19920102, WO 1992-US15 19920102; EP 567572 A1 EP 1992-904590 19920102, WO 1992-US15 19920102; JP 06502995 W JP 1992-504429 19920102, WO 1992-US15 19920102; US 5443954 A CIP of US 1987-114508 19871030, CIP of US 1988-265883 19881101, US 1991-636712 19910102

FDT AU 9212377 A Based on WO 9212258; EP 567572 A1 Based on WO 9212258; JP 06502995 W Based on WO 9212258; US 5443954 A CIP of US 4885238

PRAI US 1991-636712 19910102; US 1987-114508 19871030; US 1988-265883 19881101

AB US 7636712 A UPAB: 19960529

Disclosed are tumourigenic and non-tumourigenic **immortalised** human cell lines of bronchial and mesothelial epithelial cell origin.

USE - For identification of potential chemotherapeutic drugs, studies on the control of squamous differentiation and identification of chemical and biological agents which induce squamous differentiation, studies on metabolism of carcinogens and other xenobiotics, studies on DNA mutagenesis, studies on chromosome damaging agents, studies on malignant transformation by chemical, physical and viral agents and transferred genes including **oncogenes** and high mol. wt. genomic DNA from **tumours**, studies on cellular biochemistry, studies on cellular responses to growth factors and prodn. of growth factors, cell-cell hybrid studies for identification of **tumour** suppressor activity, prodn. of desired proteins by recombinant expression, studies on itracellular communication, characterisation of cell surface antigens and identification of novel genes. @(29pp Dwg.No.0/1)

L9 ANSWER 22 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1991-310285 [42] WPIDS

DNC C1991-134363

TI Human oesophageal epithelial cells line - used in screening for carcinogen(s) and potential chemotherapeutic agents.

DC B04 D16

IN HARRIS, C; REDDEL, R; STONER, G

PA (USSH) NAT INST OF HEALTH

CYC 1

PI US 7582060 A 19910910 (199142)*

ADT US 7582060 A US 1991-582060 19910910

PRAI US 1990-582060 19900914; US 1991-582060 19910910

AB US 7582060 A UPAB: 19930928

Human oesophageal epithelial cell line (or deriv.) is provided with a replicative capacity in cell culture which is enhanced compared to normal cells, and is unable to produce **tumours**. The cell line replicates continuously in cell culture. Also claimed are methods of testing carcinogenicity of an agent and of testing antineoplastic activity of an agent using the novel cell line, and screening kits.

In the prepn., normal human oesophageal (NHE) cells were obtd. from explant outgrowths of an autopsy specimen from a noncancerous male. Dispersed cell suspensions were plated at 3.5 x 10 power 5 cells/dish and transfected with 10 microg of plasmid pRSV-T-copptd. with strontium phosphate. After 4 hrs., the cells were shocked with glycerol. After the appearance of foci of transformed cells, control and transfected cultures were subcultured (2.5 x 10 power 5/100 mm dish). pRSV-T-Transfected cells (e.g. line designated HE-457) grew exponentially for 50 PDs, after which

it went into crisis. One separate **immortalised** cell line, designated HET-1A, was developed from the HE-457 cultures.

USE/ADVANTAGE - The cell line may be used for identification of potential carcinogens, **tumour** promoters and antagonists; for identification of potential chemotherapeutic drugs; and of anti-oesophageal cancer drugs which act by inducing terminal cell differentiation. Other applications include studies on the metabolism of carcinogens and other xenobiotics; studies of DNA mutagenesis; studies of chromosome damaging agents; studies of malignant transformation by additional **oncogenes**; and studies of cellular responses to growth factors and prodn. of growth factors. @(24pp Dwg.No 0/0)

L9 ANSWER 23 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1991-021677 [03] WPIDS
DNC C1991-009302
TI **Immortalised** human uro-epithelial cells - transformed with **SV40**, used to produce epithelial keratin(s) and for screening carcinogenic agents.
DC B04 D16
IN CHRISTIAN, B J; REZNIKOFF, C A
PA (WISC) WISCONSIN ALUMNI RES FOUND
CYC 1
PI US 4980290 A 19901225 (199103)*
ADT US 4980290 A US 1987-106310 19871009
PRAI US 1987-106310 19871009
AB US 4980290 A UPAB: 19930928
Human uroepithelial cell is claimed which is (a) established in type, (c) culture, (b) of the balanced chromosome transformed, (e) not produces epithelial keratin, (d) **SV40** spontaneously tumorigenic in an athymic nude mouse (f) transformed can be preserved cryogenically and tumourigenically and (g) from the cell line of ATCC CRL 9520. (B) Also claimed is a human uroepithelial cell that is (a) tumorigenic in an athymic nude mouse, (b) **SV40** transformed, (c) established in culture, (d) can be preserved cryogenically, (e) can produce uroepithelial keratin and (f) from the cell l1ne of ATCC CRL 9519.

USE - Cells provide a source of human epithelial related keratins. These may be used to develop antibodies for opt. diagnosis or treatment of human cancers. Also non-tumorigenic parent cells (SV-HUC-1, ATCC CRL 9520) provide a source of keratins for control purposes in antibody development and may also provide a screening host for carcinogenic agents. @(4pp Dwg.No.0/0)

L9 ANSWER 24 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-099195 [13] WPIDS
DNC C1990-043558
TI Human oesophageal epithelial cell lines - produced by transfecting normal oesophageal epithelial cells with T antigen gene of **SV40**.
DC B04 D16
IN HARRIS, C C; REDDEL, R R; STONER, G D; ROGER, R
PA (USDC) US DEPT OF COMMERCE; (USSH) US DEPT HEALTH & HUMAN SERVICE; (USDC) US SEC OF COMMERCE
CYC 17
PI US 7412802 A 19900130 (199013)* 46p
WO 9105062 A 19910418 (199118)

RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: AU CA JP
AU 9064498 A 19910428 (199131)
EP 494225 A1 19920715 (199229) EN 21p
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 04507046 W 19921210 (199304) 14p
EP 494225 A4 19930428 (199526)
ADT US 7412802 A US 1989-114778 19890927; EP 494225 A1 EP 1990-914817 19900927, WO 1990-US5462 19900927; JP 04507046 W JP 1990-513821 19900927, WO 1990-US5462 19900927; EP 494225 A4 EP 1990-914817
FDT EP 494225 A1 Based on WO 9105062; JP 04507046 W Based on WO 9105062
PRAI US 1989-412802 19890927
AB US 7412802 A UPAB: 19930928
Human epithelial cells that originate from the oseophagus and are **immortalised** in culture are disclosed.
USE/ADVANTAGE - Human esophageal epithelial cell line has a replicative capacity in cell culture that is enhanced compared to normal cells and is unable to produce **tumours**. The cell line can be used to identify carcinogens and **tumour** promoters and antagonists, identify chemotherapeutic drugs, study the metabolism of carcinogens and other xenobiotics, study DNA mutagenesis and chromosome damaging agents and for identification and purificn. of growth factors.
0/0

L9 ANSWER 25 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-085611 [12] WPIDS
DNN N1990-066015 DNC C1990-037498
TI **Immortalised** intestinal epithelial cell lines - transfected with viral or cellular **oncogene**.
DC B04 D16 S03
IN EMAMI, S; GESPACH, C P
PA (INRM) INSERM INST NAT SANTE & RECH MED
CYC 1
PI FR 2634784 A 19900202 (199012)* 22p
ADT FR 2634784 A FR 1988-10361 19880801
PRAI FR 1988-10361 19880801
AB FR 2634784 A UPAB: 19930928
New non-oncogenic **immortalised** mammalian intestinal epithelial cell lines are obtained by transfecting foetal intestinal epithelial cells with a suitable viral or cellular (proto)**oncogene**.
USE - The **immortalised** cells are useful for (a) large-scale prodn. of proteins specific to the intestinal **epithelium**, and (b) as model systems for the study and identification of biochemical systems whose expression in cell nuclei, cytoplasm or membranes is implicated in the proliferation and differentiation of intestinal epithelial cells.
0/2

L9 ANSWER 26 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1989-263488 [36] WPIDS
CR 1988-036306 [05]; 1988-147442 [21]; 1991-368903 [50]; 1993-351737 [44]; 1995-035935 [05]
DNC C1989-116974
TI **Immortalised** human bronchial epithelial and mesothelial cell lines - contain no **oncogene** and are able to grow in serum free

media, used as gene recipients and for chemical testing, etc..
DC B04 D16
IN HARRIS, C C
PA (USSH) US DEPT HEALTH & HUMAN SERVICE
CYC 1
PI US 7265883 A 19890627 (198936)* 22p
ADT US 7265883 A US 1988-265883 19881101
PRAI US 1988-265883 19881101
AB US 7265883 A UPAB: 19960529
Immortalised but non-tumorigenic human bronchial epithelical and human mesothelial cell lines are new.
USE/ADVANTAGE - These cell lines do not contain an **oncogene**, have unlimited proliferative potential and can grow in the same serum-free media as normal cells. They are useful as recipients for other **oncogenes** and for testing cpds. for cyclotoxicity, growth inhibition, growth promotion, squamous differentiation, etc..
0/0
Dwg.0/0

L9 ANSWER 27 OF 27 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1989-150769 [20] WPIDS
DNC C1989-066778
TI In vitro prodn. of **immortalised** neural precursor cells - by infecting neuro-epithelial or neural crest cells with retro-viral vector carrying MCY **oncogene**.
DC B04 D16
IN BARTLETT, P F; BERNARD, O
PA (AMRA-N) AMRAD CORP LTD
CYC 6
PI WO 8903872 A 19890505 (198920)* EN 46p
AU 8824480 A 19890504 (198926)
ZA 8808100 A 19891227 (199005)
EP 383804 A 19900829 (199035)
JP 03504917 W 19911031 (199150)
CA 1312839 C 19930119 (199309)
EP 383804 B1 19941130 (199501) EN 25p
DE 3852314 G 19950112 (199507)
US 5580777 A 19961203 (199703) 17p
ADT WO 8903872 A WO 1988-AU423 19881028; ZA 8808100 A ZA 1988-8100 19881028; EP 383804 A EP 1988-909272 19881028; JP 03504917 W JP 1988-508569 19881028; CA 1312839 C CA 1988-581556 19881028; EP 383804 B1 EP 1988-909272 19881028, WO 1988-AU423 19881028; DE 3852314 G DE 1988-3852314
19881028, EP 1988-909272 19881028, WO 1988-AU423 19881028; US 5580777 A Cont of WO 1988-AU423 19881028, Cont of US 1992-935357 19920827, US 1994-330114 19941027
FDT EP 383804 B1 Based on WO 8903872; DE 3852314 G Based on EP 383804, Based on WO 8903872
PRAI AU 1987-5131 19871029; AU 1988-24480 19881028
AB WO 8903872 A UPAB: 19930923
In vitro prodn. of **immortalised** neural precursor cells comprises infecting neuroepithelial or neural crest cells with a retroviral vector carrying a myc **oncogene**. Also claimed are the **immortalised** or continuous cell lines carrying the vector.
USE - The retroviral cells express cytokeratin but not neuronal or glial cell markers, and can be induced to express class I histocompatibility antigens on stimulation with interferon-8.. Although

unable to spontaneously differentiate in vitro, exposure to basic fibroblast growth factor induces their differentiation into neurofilaments positive neutrons and glial fibrillary acids protein positive glial cells.

Different types of mouse neuroepithelial and neural crest cell lines can be generated by introducing different vectors and some are capable of spontaneously differentiating in vitro into neural and/or glial cells. Many of these cell lines are factor dependent and can be used as target populations to rapidly screen for the potential neurotropic factors, and for prodn. of factors important for maintenance and replication of cells in the central and peripheral nervous systems. The **immortalised** cell lines may be used as a modal system to study the possibility of using cell lines to restore brain damage after an accident, stroke, or in diseases such as Parkinson. Huntington and ALzheimers.

0/8

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=> fil medline

FILE 'MEDLINE' ENTERED AT 10:54:34 ON 21 DEC 2000

 FILE LAST UPDATED: 27 OCT 2000 (20001027/UP).  FILE COVERS 1960 TO DATE.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2000 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

 MEDLINE UPDATES ARE ON HOLD UNTIL AFTER THE ANNUAL RELOAD HAS BEEN
 COMPLETED.  NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND
 RELOAD DETAILS WILL BE FOUND IN HELP RLOAD.

=> d his


     (FILE 'MEDLINE' ENTERED AT 09:49:46 ON 21 DEC 2000)
                DEL HIS Y
L1           34 S (IMMORTALIZ? AND EPITHELIAL AND SV40)/TI

     FILE 'STNGUIDE' ENTERED AT 10:10:07 ON 21 DEC 2000

     FILE 'MEDLINE' ENTERED AT 10:30:05 ON 21 DEC 2000
L2            0 S L1 AND BONE MARROW
L3       143222 S EPITHELIUM+NT/CT
L4         9669 S POLYOMAVIRUS MACACAE+NT/CT
L5          305 S L3 AND L4
L6            0 S CELL TRANSFORMATION, VIRAL+NT/CFT
L7        11638 S CELL TRANSFORMATION, VIRAL+NT/CT
L8            0 S L5 AND L6
L9          133 S L5 AND L7
                E IMMUNOSTIMUL/CT
                E E7+ALL
                E IMMUNOSTIMUL/CT
                E E5+ALL
                E IMMUNOSTIMUL/CT
                E E4+ALL
                E ADJUVANTS, IMMUNOLOGIC/CT
                E E3=ALL
                E ADJUVANTS, IMMUNOLOGIC/CT
                E E3+ALL
L10       76403 S ADJUVANTS, IMMUNOLOGIC+NT/CT
L11           2 S L9 AND L10
L12       59365 S BONE MARROW+NT/CT
L13           0 S L12 AND L9
L14           1 S L5 AND L12
                E ONCOGENES/CT
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                E E3+ALL
L15         29691 S ONCOGENES+NT/CT
L16            13 S L15 AND L9
                E IMMORTALIZ/CT
                E E2+ALL
                E METAST/CT
                E E4+ALL
                E NEOPLASM METASTASIS+NT/CT
L17         81789 S NEOPLASM METASTASIS+NT/CT
L18             2 S L17 AND L9
L19           104 S IMMORTALIZ? AND L5
L20            41 S L19 AND L7
L21            10 S L20 AND (L15 OR L10 OR L12)
L22             0 S CELL TRANSFORMATION/CT
                E CELL TRANSFORMATION/CT
                E E4+ALL
                E CELL TRANSFORMATION, VIRAL/CT
                E E3+ALL
L23         30312 S CELL TRANSFORMATION, NEOPLASTIC+NT/CT
L24            79 S L23 AND L5
L25            25 S L24 AND (L15 OR L10 OR L12 OR L17)
L26            15 S L16 OR L18 OR L14 OR L21
L27            14 S L25 NOT L26

     FILE 'MEDLINE' ENTERED AT 10:54:34 ON 21 DEC 2000

=> d .med 1-15 l26;d .med l27 1-14


L26  ANSWER 1 OF 15  MEDLINE
AN   1999343007     MEDLINE
DN   99343007
TI   Urothelium-specific expression of an oncogene in transgenic mice induced
     the formation of carcinoma in situ and invasive transitional cell
     carcinoma.
AU   Zhang Z T; Pak J; Shapiro E; Sun T T; Wu X R
CS   Department of Urology, Kaplan Comprehensive Cancer Center, New York
     University School of Medicine, New York 10016, USA.
NC   DK39753 (NIDDK)
     DK49469 (NIDDK)
     DK52206 (NIDDK)
SO   CANCER RESEARCH, (1999 Jul 15) 59 (14) 3512-7.
     Journal code: CNF. ISSN: 0008-5472.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; Cancer Journals
EM   199910
EW   19991002
AB   Although many genetic alterations are known to be associated with human
     transitional cell carcinoma (TCC) of the urinary bladder, relatively
     little is known about the roles of these molecular defects, singular or
in
     combination, in bladder tumorigenesis. We have developed a transgenic
     mouse model of bladder tumorigenesis using a 3.6-kb promoter of uroplakin
     II gene to drive the urotheliums-specific expression of oncogenes. In
this
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study, we demonstrate that transgenic mice bearing a low copy number of SV40T transgene developed bladder carcinoma in situ (CIS), whereas those bearing high copies developed CIS as well as invasive and metastatic TCCs.

These results indicate that the SV40T inactivation of p53 and retinoblastoma gene products, defects frequently found in human bladder CIS and invasive TCCs, can cause the aggressive form of TCC. Our results also provide experimental proof that CIS is a precursor of invasive TCCs, thus supporting the concept of two distinct pathways of bladder tumorigenesis (papillary versus CIS/invasive TCC). This transgenic system can be used for the systematic dissection of the roles of individual or combinations of specific molecular events in bladder tumorigenesis.

CT Check Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Antigens, Polyomavirus Transforming: BI, biosynthesis
*Antigens, Polyomavirus Transforming: GE, genetics
*Bladder Neoplasms: GE, genetics
Bladder Neoplasms: PA, pathology
*Carcinoma in Situ: GE, genetics
Carcinoma in Situ: PA, pathology
Carcinoma, Papillary: GE, genetics
*Carcinoma, Transitional Cell: GE, genetics
Carcinoma, Transitional Cell: PA, pathology
*Cell Transformation, Neoplastic: GE, genetics
Cell Transformation, Viral: GE, genetics
Gene Expression Regulation, Neoplastic
Genes, p53
Genes, Retinoblastoma
*Membrane Proteins: GE, genetics
Mice
Mice, Transgenic
Neoplasm Invasiveness
Neoplasm Metastasis
Neoplasm Proteins: BI, biosynthesis
Neoplasm Proteins: GE, genetics
***Oncogenes**
Organ Specificity
Polyomavirus macacae: GE, genetics
Promoter Regions (Genetics)
Recombinant Fusion Proteins: BI, biosynthesis
*Transgenes
***Urothelium: ME, metabolism**

L26 ANSWER 2 OF 15 MEDLINE
AN 1999054658 MEDLINE
DN 99054658
TI Tumors of the retinal pigment epithelium metastasize to inguinal lymph nodes and spleen in tyrosinase-related protein 1/SV40 T antigen transgenic mice.
AU Penna D; Schmidt A; Beermann F
CS Swiss Institute for Experimental Cancer Research (ISREC), Epalinges.
SO ONCOGENE, (1998 Nov 19) 17 (20) 2601-7.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals; Cancer Journals
EM 199902
EW 19990204
AB The pigment epithelium of the retina (RPE) is derived from the optic cup and is essential for function and development of the eye. We produced a transgenic mouse line that expresses simian virus (SV40) transforming sequences under control of the 1.4 kb tyrosinase-related protein 1 (TRP-1) promoter, targeting expression of T antigen (Tag) to the RPE. In transgenic embryos, RPE cells proliferated in the anterior part of the eye and near the optic nerve. This resulted in formation of tumors, which were pigmented and of epithelial origin. In 3 months-old mice, pigmented cells were detected in spleen and inguinal lymph nodes. In spleen, tyrosinase, TRP-1 and SV40 Tag were expressed and tyrosinase was enzymatically active. Pigmented regions were positive for an epithelial marker, cytokeratin. Cell lines were established from tumor and metastases and kept in culture for more than 2 months. These were pigmented, and maintained expression of tyrosinase, TRP-1, cytokeratin and SV40 Tag. This demonstrates that RPE tumor cells metastasize to lymph node and spleen. In conclusion, the metastasis from TRP-1/Tag RPE tumors towards spleen and lymph nodes serves as potential tool to investigate biology and metastasis of tumors derived from the pigment epithelium.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Antigens, Polyomavirus Transforming: GE, genetics
*Antigens, Polyomavirus Transforming: PH, physiology
Cell Transformation, Neoplastic
Cell Transformation, Viral
Epithelial Cells: PA, pathology
Gene Expression Regulation, Developmental
Groin
***Lymphatic Metastasis**
Melanins: BI, biosynthesis
Mice
Mice, Inbred BALB C
Mice, Transgenic
Organ Specificity
Pigment Epithelium of Eye: EM, embryology
***Pigment Epithelium of Eye: PA, pathology**
Pigmentation
Polyomavirus macacae: GE, genetics
Promoter Regions (Genetics)
*Proteins: GE, genetics
Recombinant Fusion Proteins: PH, physiology
Retinal Neoplasms: ET, etiology
*Retinal Neoplasms: PA, pathology
*Splenic Neoplasms: PA, pathology

L26 ANSWER 3 OF 15 MEDLINE
AN 97376990 MEDLINE
DN 97376990
TI Activation of the focal adhesion kinase signal transduction pathway in cervical carcinoma cell lines and human genital epithelial cells

immortalized with human papillomavirus type 18.
AU McCormack S J; Brazinski S E; Moore J L Jr; Werness B A; Goldstein D J
CS The Vincent T Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC 20007, USA.
NC IP50CA58185 (NCI)
R29 CA-63044 (NCI)
SO ONCOGENE, (1997 Jul 17) 15 (3) 265-74.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199710
EW 19971004
AB The inappropriate activation of protein-tyrosine kinases (PTKs) has been associated with initiation and progression of several types of human cancers. We therefore postulated that **immortalization** by DNA tumor viruses results in the induction of PTKs fundamental to these processes. An RT-PCR-based screen was thus used to identify PTKs that were abundantly expressed in HPV-18-**immortalized** epithelial cells and HPV-containing carcinoma cell lines. One of the genes isolated in this screen was the focal adhesion kinase (FAK; pp125FAK), a cytoplasmic protein kinase that is activated in v-src transformed cells or by stimulation with mitogenic polypeptides. FAK also becomes catalytically active upon integrin engagement with extracellular matrix proteins, such as fibronectin. We found that FAK expression and activity were significantly elevated in HPV-18 E6/E7-**immortalized** human genital epithelial cells relative to their primary cell counterparts. Protein expression and tyrosine phosphorylation of the putative FAK substrate, paxillin, were also notably increased upon HPV-18 **immortalization** of genital epithelial cells and in HPV-containing cervical carcinoma cell lines. Most significantly, these cells expressed markedly higher levels of both intracellular and extracellular fibronectin, thus providing a mechanism for activation of FAK and increased tyrosine phosphorylation of paxillin. These findings suggest a role for the integrin/FAK-mediated signaling pathway in cervical carcinogenesis and represent one of the first demonstrations of a tyrosine kinase whose activity is elevated following viral **immortalization**.
CT Check Tags: Female; Human; Support, U.S. Gov't, P.H.S.
Cell Adhesion Molecules: BI, biosynthesis
*Cell Adhesion Molecules: ME, metabolism
*Cell Transformation, Neoplastic
***Cell Transformation, Viral**
Cells, Cultured
*Cervix Neoplasms: PA, pathology
Cervix Neoplasms: PP, physiopathology
*Cervix Uteri: CY, cytology
Cervix Uteri: PA, pathology
Cytoskeletal Proteins: BI, biosynthesis
Epithelium: PH, physiology
***Genes, src**
Keratinocytes: CY, cytology
Keratinocytes: PH, physiology
*Papillomavirus, Human: GE, genetics

Papillomavirus, Human: PH, physiology
Phosphoproteins: BI, biosynthesis
Phosphorylation
Polymerase Chain Reaction
Polyomavirus macacae: GE, genetics
*Protein-Tyrosine Kinase: ME, metabolism
*Signal Transduction
Tumor Cells, Cultured

L26 ANSWER 4 OF 15 MEDLINE
AN 97163640 MEDLINE
DN 97163640
TI Characterization of a newly established human bone marrow endothelial cell line: distinct adhesive properties for hematopoietic progenitors compared with human umbilical vein endothelial cells.
AU Schweitzer K M; Vicart P; Delouis C; Paulin D; Drager A M; Langenhuijsen M M; Weksler B B
CS Department of Hematology, Free University Hospital Amsterdam, The Netherlands.
NC HL-18828 (NHLBI)
SO LABORATORY INVESTIGATION, (1997 Jan) 76 (1) 25-36.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199705
EW 19970501
AB Human bone marrow endothelial cells (HBMEC) are intimately involved in the homing of hematopoietic progenitor cells (HPC) to the bone marrow and in the regulation of proliferation and differentiation of these cells. Because availability of primary HBMEC and their capacity to be cultured in vitro are limited, we used isolated HBMEC to establish a cloned cell line by microinjection of a recombinant plasmid expressing simian virus 40 early genes under the control of a deletion mutant of the human vimentin promoter. Serum requirements for growth of a transformed HBMEC line (TrHBMEC) were markedly decreased compared with those of primary cells, and added growth factors were not required for proliferation. Cells took up acetylated low-density lipoprotein normally, bound to Ulex europaeus lectin, and stained positively for von Willebrand factor, P-selectin, CD31, CD34, CD44, very late antigen-5, and intercellular adhesion molecule-2 (ICAM-2). After treatment with TNF-alpha or lipopolysaccharide, TrHBMEC increased surface expression of E-selectin, vascular cell adhesion molecule-1 (VCAM-1), and ICAM-1 in a manner similar to primary HBMEC. In contrast, IL-1 beta elicited much less up-regulation of these adhesion molecules than in primary cells. In previous work, we reported that, in a flow adhesion model, rolling of peripheral blood CD34+ cells on primary HBMEC was E-selectin-dependent, whereas VCAM-1 and ICAM-1 contributed to firm adhesion. In the present study, we show that HPC adhere in a similar way to TrHBMEC. A less-pronounced role for VCAM-1 and ICAM-1 was found in the adhesion of HPC to human umbilical vein endothelial cells.

Furthermore, significantly more CD34+ cells adhered to TNF-alpha-stimulated HBMEC and TrHBMEC than to similarly stimulated human umbilical vein endothelial cells. These data emphasize the importance of using microvessel HBMEC for studying the homing of HPC to the bone marrow, and indicate the usefulness of the above-described bone marrow endothelial cell line.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigens, CD: AN, analysis
*Antigens, CD: BI, biosynthesis
Antigens, CD34: AN, analysis
Antigens, Viral, Tumor: BI, biosynthesis
***Bone Marrow: CY, cytology**
Bone Marrow: PH, physiology
Cell Adhesion
Cell Adhesion Molecules: AN, analysis
*Cell Adhesion Molecules: BI, biosynthesis
Cell Line
Clone Cells
***Endothelium: CY, cytology**
Endothelium: PH, physiology
Endothelium, Vascular: CY, cytology
***Endothelium, Vascular: PH, physiology**
Flow Cytometry
Hematopoietic Stem Cells: CY, cytology
*Hematopoietic Stem Cells: PH, physiology
IgG
Polyomavirus macacae: GE, genetics
Regulatory Sequences, Nucleic Acid
Tissue Culture: MT, methods
Transfection
Umbilical Veins
Vimentin: BI, biosynthesis

L26 ANSWER 5 OF 15 MEDLINE
AN 96029180 MEDLINE
DN 96029180
TI Recurrent cytogenetic alterations of prostate carcinoma and amplification of c-myc or epidermal growth factor receptor in subclones of **immortalized** PNT1 human prostate epithelial cell line.
AU Degeorges A; Hoffschir F; Cussenot O; Gauville C; Le Duc A; Dutrillaux B; Calvo F
CS Laboratoire de Pharmacologie, Institut de Genetique Moleculaire, Hopital Saint-Louis, Paris, France.
SO INTERNATIONAL JOURNAL OF CANCER, (1995 Sep 15) 62 (6) 724-31.
Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199601
AB To develop an experimental prostate cancer model, we **immortalized** normal human prostate adult epithelial cells with SV40 large-T antigen. Two sublines were derived in culture, namely PNT1A and PNT1B. They retained the characteristics of prostate epithelial cells, but did not

clone in soft agarose. PNT1A occasionally formed undifferentiated adenocarcinoma tumors in nude mice, but only in the presence of matrigel. PNT1A and PNT1B displayed common cytogenetic alterations: a 10q arm deletion, which is a recurrent alteration in prostate carcinoma, chromosome losses and a translocation involving chromosome 5. An extensive study of oncogenic alterations occurring in these cells showed that PNT1A displayed c-myc gene amplification, forming an hsr on chromosome 4, as well as gene amplification, forming an hsr on chromosome 4, as well as c-myc mRNA overexpression, with a faster doubling time (25 hr); moreover, it seemed less sensitive to EGF than PNT1B. PNT1B had a doubling time identical to that of normal cells (48 hr) but displayed EGF receptor gene amplification accompanied by an increased number of EGF binding sites and sensitivity to EGF. Because both cell lines displayed cytogenetic and oncogenic alterations found in prostate cancer, as well as differing malignant potentials, they represent an interesting model for studying the progression of prostate tumors.

CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
Adult
Base Sequence
Cell Division: PH, physiology
***Cell Transformation, Viral**
Epithelium: PA, pathology
*Gene Amplification
***Genes, myc**
Karyotyping
Mice
Mice, Nude
Molecular Sequence Data
Neoplasm Transplantation
Phenotype
Polyomavirus macacae
*Prostatic Neoplasms: GE, genetics
Prostatic Neoplasms: PA, pathology
Prostatic Neoplasms: UL, ultrastructure
*Receptor, Epidermal Growth Factor: GE, genetics
Tumor Cells, Cultured

L26 ANSWER 6 OF 15 MEDLINE
AN 95221047 MEDLINE
DN 95221047
TI SV40-induced **immortalization** and ras-transformation of human bronchial epithelial cells.
AU Reddel R R; De Silva R; Duncan E L; Rogan E M; Whitaker N J; Zahra D G; Ke Y; McMenamin M G; Gerwin B I; Harris C C
CS Children's Medical Research Institute, Westmead, Sydney, NSW, Australia..
SO INTERNATIONAL JOURNAL OF CANCER, (1995 Apr 10) 61 (2) 199-205. Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199507
AB Non-tumorigenic SV40-**immortalized** human cells may be transformed

to tumorigenicity by activated oncogenes, but the molecular genetics of this process are still poorly understood. We describe here 4SV40-transformed bronchial epithelial (BE) cell lines that became **immortalized** after a period of crisis, and then transfection of 6 BE lines or sub-lines with an activated c-Ha-ras (EJ-ras) oncogene. pSV2neo-transfected cells did not form any tumors in athymic nude mice. Even though each of the EJ-ras-transfected lines was shown to be expressing the mutant ras gene, only one cell line, BEAS-2B, and 2 of its sub-lines were tumorigenic after transfection. We conclude that **immortalization** is not sufficient for BE cells to be transformed by the EJ-ras oncogene. Thus there are at least 2 unknown genetic events in this in vitro model of carcinogenesis: escape from crisis (**immortalization**), and development of ability to cooperate with activated ras in tumorigenic transformation. We found no evidence that either **immortalization** or ability to complement ras is related to abnormalities of the SV40 T antigens, of p110RB or of p53.

CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
Antigens, Polyomavirus Transforming: ME, metabolism
Base Sequence
Bronchi: CY, cytology
Bronchi: ME, metabolism
*Bronchi: PH, physiology
Cell Line
*Cell Transformation, Neoplastic: GE, genetics
***Cell Transformation, Viral: GE, genetics**
Codon
Epithelium: CY, cytology
Epithelium: ME, metabolism
Epithelium: PH, physiology
Gene Expression
Gene Expression Regulation, Neoplastic
Genes, p53
***Genes, ras**
Genetic Complementation Test
Mice
Mice, Nude
Molecular Sequence Data
Phosphorylation
Polymorphism (Genetics)
***Polyomavirus macacae: GE, genetics**
Precipitin Tests
Retinoblastoma Protein: ME, metabolism
Transfection

L26 ANSWER 7 OF 15 MEDLINE
AN 93330547 MEDLINE
DN 93330547
TI Expression of epithelial phenotype is enhanced by v-Ha-ras in rat endometrial cells **immortalized** by SV40 T antigen.
AU Helftenbein G; Alvarez C V; Tuohimaa P; Beato M
CS Institut fur Molekularbiologie und Tumorforschung (IMT), Philipps Universitat, Marburg, Germany..
SO ONCOGENE, (1993 Aug) 8 (8) 2075-85.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals; Cancer Journals
EM 199310
AB To study the interplay of steroid hormones and oncogenes in the control of endometrial cell proliferation and differentiation we have generated cell lines derived from rat endometrium by expressing the **immortalizing** oncogenes adeno E1A or SV40 large T antigen. These lines are positive for mesenchymal markers and contain very few characteristic epithelial proteins. Cell lines expressing a temperature-sensitive mutant of SV40 T antigen exhibit a temperature-dependent morphology and growth behavior, but do not manifest an epithelial phenotype at the non-permissive temperature. Cell lines additionally infected with retroviral vectors carrying the v-Ha-ras oncogene (p21rasArg-12) no longer express collagen type III and recover part of their epithelial potential by expressing cytokeratins and/or cadherin E. Some of these cells also express characteristic decidual marker proteins such as desmin, whereas others express glandular epithelial markers such as uteroglobin. Uteroglobin mRNA levels in these cells are increased by glucocorticoids. The parental temperature-sensitive cells do not contain progesterone receptor but become positive for progesterone receptor at the permissive temperature after infection with the v-Ha-ras-expressing retrovirus. Our results indicate that there is a fluent transition and overlapping between mesenchymal, glandular epithelial and decidual phenotypes of endometrial cells, suggesting that these three cell types are derived from the same stem/precursor cells. The v-Ha-ras oncogene product appears to act on the differentiation pathway at an early step prior to the distinction between decidual and glandular epithelial lineage.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
*Antigens, Polyomavirus Transforming: GE, genetics
Base Sequence
Cell Adhesion Molecules: AN, analysis
*Cell Differentiation
Cell Line, Transformed
***Cell Transformation, Viral**
*Endometrium: CY, cytology
Epithelium: CY, cytology
***Genes, ras**
Molecular Sequence Data
Phenotype
***Polyomavirus macacae: IM, immunology**
Rats
Receptors, Progesterone: AN, analysis
RNA, Messenger: AN, analysis
Uteroglobin: GE, genetics

L26 ANSWER 8 OF 15 MEDLINE
AN 92223016 MEDLINE
DN 92223016
TI Losses of 3p, 11p, and 13q in EJ/ras-transformable simian virus 40-**immortalized** human uroepithelial cells.
AU Kao C; Wu S Q; Bhatthacharya M; Meisner L F; Reznikoff C A
CS Department of Biochemistry, University of Wisconsin, Madison 53792..
NC RO1-CA29525-11 (NCI)
P01-CA51987 (NCI)
SO GENES, CHROMOSOMES AND CANCER, (1992 Mar) 4 (2) 158-68.
Journal code: AYV. ISSN: 1045-2257.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
AB Five independent clones of Simian virus 40 (SV40)-**immortalized** human uroepithelial cells (CK/SV-HUC) were established after transfection of HUC cultures from the same tissue donor with plasmids encoding SV40 large T and small t antigen genes. Each CK/SV-HUC clone contained a unique SV40 integration site, and all expressed similar levels of SV40 mRNA. All five clones were nontumorigenic, but clones 2, 4, and 5 tumorigenically transformed after transfection at P19 with mutant EJ/ras and also spontaneously after 40 serial passages in vitro. In contrast, CK/SV-HUC clones 1 and 3 did not transform when either approach was used. These differences in transformability among CK/SV-HUC clones could not be predicted based on differences in SV40 gene expression nor on any in vitro growth property tested. In cytogenetic analyses, a transformable clone showed losses of three chromosome arms containing putative cancer suppressor gene regions, including 3p14----pter, 13q, and 11p, whereas the nontransformable clones showed none of these losses. Thus these data indicate that genetic losses on 3p, 11p, and 13q may contribute to tumorigenic transformation of SV40-**immortalized** human uroepithelial cells.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Bladder Neoplasms: GE, genetics
Cell Division
Cell Line, Transformed
*Cell Transformation, Neoplastic: GE, genetics
***Cell Transformation, Viral: GE, genetics**
*Chromosome Deletion
Chromosomes, Human, Pair 11
Chromosomes, Human, Pair 13
Chromosomes, Human, Pair 3
Epithelium: PA, pathology
***Genes, ras: PH, physiology**
Karyotyping
Polyomavirus macacae
Transfection

L26 ANSWER 9 OF 15 MEDLINE
AN 90352619 MEDLINE
DN 90352619
TI Evidence for the multistep nature of in vitro human epithelial cell carcinogenesis.
AU Rhim J S; Yoo J H; Park J H; Thraves P; Salehi Z; Dritschilo A
CS Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland 20892..
SO CANCER RESEARCH, (1990 Sep 1) 50 (17 Suppl) 5653S-5657S.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199011

AB In keeping with the multistep development of human cancer in vivo, a stepwise approach to neoplastic transformation in vitro presents a reasonable strategy. We have recently developed an in vitro multistep model suitable for the study of human epithelial cell carcinogenesis. Upon infection with the adenovirus 12-simian virus 40 hybrid virus, primary human epidermal keratinocytes acquired an indefinite life span in culture but did not undergo malignant conversion. Subsequent addition of Kirsten murine sarcoma virus and human ras oncogene or chemical carcinogens (N-methyl-N'-nitro-N-nitrosoguanidine or 4-nitroquinoline 1-oxide) to these cells induced morphological alterations and the acquisition of neoplastic properties. Subsequently it was found that this line could be transformed neoplastically by a variety of retrovirus-containing H-ras, bas, fes, fms, erbB, and src oncogenes. In addition, we found that the **immortalized** human epidermal keratinocyte (RHEK-1) line can be transformed neoplastically by exposure to ionizing radiation. Thus, this in vitro system may be useful in studying the interaction of a variety of carcinogenic agents and human epithelial cells. These findings demonstrate the malignant transformation of human primary epithelial cells in culture by the combined action of viruses, oncogenes, chemical carcinogens, or X-ray irradiation and support a multistep process for neoplastic conversion.

CT Check Tags: Human
Adenoviridae: GE, genetics
Cell Line
*Cell Transformation, Neoplastic
Cell Transformation, Viral
Epithelium: PA, pathology
Epithelium: RE, radiation effects
Gene Expression Regulation
Genes, ras
Polyomavirus macacae: GE, genetics

L26 ANSWER 10 OF 15 MEDLINE
AN 89273891 MEDLINE
DN 89273891
TI Neoplastic transformation of a human bronchial epithelial cell line by a recombinant retrovirus encoding viral Harvey ras.
AU Amstad P; Reddel R R; Pfeifer A; Malan-Shibley L; Mark G E 3d; Harris C C
CS Division of Cancer Etiology, National Cancer Institute, Bethesda, Maryland 20892.
SO MOLECULAR CARCINOGENESIS, (1988) 1 (3) 151-60.
Journal code: AEQ. ISSN: 0899-1987.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198909
AB Activated ras oncogenes have previously been implicated in the pathogenesis of human lung carcinomas. A v-Ha-ras-containing retrovirus, Zip-ras, was generated by inserting the coding region of the v-Ha-ras oncogene into the Zip-NeoSV(X) [Cepko et al., Cell 37:1053-1062, 1984] retroviral vector. Amphotrophic Zip-ras retrovirus was used to infect an SV40 large T antigen-positive **immortalized** cell line, BEAS-2B, derived from normal bronchial epithelial cells, the predominant progenitor

cells of human lung carcinomas. Zip-ras-infected BEAS-2B cells selected for G418 resistance formed anaplastic carcinomas in 12 of 15 athymic nude mice (latency 3 wk), whereas Zip-NeoSV(X)-infected BEAS-2B control cultures inoculated into 12 nude mice formed no tumors after a minimum of 7 mo. Tumor cell lines were established and demonstrated to be of human epithelial origin and to express v-Ha-ras p21 protein. A common feature of the tumor cell lines was an increase in ploidy. The increased efficiency of neoplastic transformation by v-Ha-ras of cell lines as compared with our previous results with normal bronchial epithelial cells [Yoakum et al., Science 227:1174-1179, 1985] is consistent with the hypothesis that the **"immortalization"** step is rate-limiting in in vitro human epithelial cell carcinogenesis.

CT Check Tags: Animal; Human
*Bronchi: CY, cytology
Bronchial Neoplasms: PA, pathology
Carcinogenicity Tests
Cell Line
*Cell Transformation, Neoplastic: GE, genetics
Cell Transformation, Viral
Epithelium: CY, cytology
***Genes, ras**
Isoenzymes
Mice
Mice, Nude
Polyomavirus macacae: GE, genetics
Recombination, Genetic
Tumor Cells, Cultured: PA, pathology

L26 ANSWER 11 OF 15 MEDLINE
AN 89069672 MEDLINE
DN 89069672
TI Cooperation of V-oncogenes in human epithelial cell transformation.
AU Rhim J S; Kawakami T; Pierce J; Sanford K; Arnstein P
CS Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland..
SO LEUKEMIA, (1988 Dec) 2 (12 Suppl) 151S-159S.
Journal code: LEU. ISSN: 0887-6924.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198903
AB The development of tissue culture systems for propagation of human epithelial cells has aided the investigation of events that lead epithelial cells to become neoplastic. In the present study, nontumorigenic human epidermal keratinocytes, **immortalized** by Ad12-SV40 virus or pSv3-neo, were transformed by a variety of retroviruses containing bas, H-ras, fes, fms, erbB and src oncogenes. Such transformants showed morphological alterations and induced carcinomas when transplanted into nude mice. These findings demonstrate the malignant transformation of human primary epithelial cells in culture by the combined action of Ad12-SV40 virus and retroviral oncogenes and support a multistep process for neoplastic conversion. This in vitro system may be useful in studying the interaction of a variety of retroviral oncogenes

and human epithelial cells.
CT Check Tags: Animal; Human
Adenoviridae: GE, genetics
*Adenoviridae: PH, physiology
*Cell Transformation, Neoplastic: GE, genetics
***Cell Transformation, Viral**
Cells, Cultured
***Epithelium: PA, pathology**
*Genes, Viral
Mice
Mice, Nude
Oncogene Proteins, Viral: GE, genetics
Oncogene Proteins, Viral: PH, physiology
***Oncogenes**
Polyomavirus macacae: GE, genetics
***Polyomavirus macacae: PH, physiology**
Retroviridae: GE, genetics
*Retroviridae: PH, physiology

L26 ANSWER 12 OF 15 MEDLINE
AN 88320361 MEDLINE
DN 88320361
TI Characterization of human tracheal epithelial cells transformed by an origin-defective simian virus 40.
AU Gruenert D C; Basbaum C B; Welsh M J; Li M; Finkbeiner W E; Nadel J A
CS Cardiovascular Research Institute, University of California, San Francisco
94143.
NC HL24136 (NHLBI)
HL 29851 (NHLBI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1988 Aug) 85 (16) 5951-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198812
AB To facilitate understanding of the mechanisms underlying pulmonary diseases, including lung cancer and cystic fibrosis, we have transformed and characterized cultures of human tracheal epithelial cells. Cells were transfected by calcium phosphate precipitation with a plasmid containing a
replication-defective simian virus 40 (SV40) genome. Colonies of cells with enhanced growth potential were isolated and analyzed for transformation- and epithelial-specific characteristics. Precrisis cells were observed to express the SV40 large tumor antigen, produce cytokeratins, have microvilli, and form tight junctions. After crisis, cells continued to express the SV40 large tumor antigen as well as epithelial-specific cytokeratins and to display the apical membrane microvilli. Apical membrane Cl channels were opened in postcrisis cells exposed to 50 microM forskolin. These channels showed electrical properties similar to those observed in primary cultures. The postcrisis cells have been in culture for greater than 250 generations and are potentially "immortal." In addition to providing a useful in vitro model for the study of ion transport by human airway epithelial cells, the cells

can be used to examine stages of neoplastic progression.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Line, Transformed
*Cell Transformation, Neoplastic
***Cell Transformation, Viral**
Chlorides: ME, metabolism
Defective Viruses
Epithelium: ME, metabolism
Epithelium: PA, pathology
Ion Channels: PH, physiology
Keratin: AN, analysis
Oncogenes
Polyomavirus macacae
Trachea: ME, metabolism
*Trachea: PA, pathology

L26 ANSWER 13 OF 15 MEDLINE
AN 87064487 MEDLINE
DN 87064487
TI Establishment of two rabbit mammary epithelial cell lines with distinct oncogenic potential and differentiated phenotype after microinjection of transforming genes.
AU Garcia I; Sordat B; Rauccio-Farinon E; Dunand M; Kraehenbuhl J P; Diggelmann H
SO MOLECULAR AND CELLULAR BIOLOGY, (1986 Jun) 6 (6) 1974-82.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198703
AB The goal of this work was to establish an assay for transformation of epithelial cells. Two epithelial cell lines were obtained after microinjecting transforming genes into primary rabbit mammary secretory cells. The cell lines were analyzed for their oncogenic potential and for the maintenance of a differentiated phenotype. A fully transformed cell line, which retained epithelial cell organization, was obtained by coinjecting simian virus 40 DNA and the activated human c-Ha-ras gene. The proliferation rate of these cells was high, with a doubling time of 16 h. Their growth was anchorage independent, and they had lost contact inhibition. The cells were tumorigenic in nude mice, but had no metastatic potential. Both microinjected DNAs were efficiently transcribed and translated, in contrast to the casein genes, which were expressed in primary cells but not in the transformed cell line. An **immortalized** cell line established after injection with simian virus 40 DNA alone was characterized by a moderate rate of proliferation with a doubling time of approximately 30 h. The growth of these cells was contact inhibited and anchorage dependent. The cells were not tumorigenic in nude mice. The viral DNA was expressed during early passages, as shown by the presence of the large T antigen in cell nuclei, but not at later passages. A high number of lactogenic hormone receptors were found associated with the cell surface. Despite the presence of these receptors, no induction of genes coding for milk proteins was observed after addition

of prolactin. These data demonstrate that this assay system can be used to
assess the **immortalizing** and transforming potential of candidate oncogenes in epithelial cells.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Caseins: GE, genetics
Cell Differentiation
Cell Line
***Cell Transformation, Viral**
DNA, Neoplasm: GE, genetics
DNA, Viral: GE, genetics
Epithelium: CY, cytology
Gene Expression Regulation
*Mammae: CY, cytology
Microscopy, Electron
Neoplasms, Experimental: GE, genetics
***Oncogenes**
Polyomavirus macacae
Rabbits

L26 ANSWER 14 OF 15 MEDLINE
AN 86216161 MEDLINE
DN 86216161
TI In vitro transformation of human epithelial cells.
AU Chang S E
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1986) 823 (3) 161-94. Ref: 212
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals; Cancer Journals
EM 198609
CT Check Tags: Animal; Comparative Study; Female; Human; Male
Antigens, Viral, Tumor: PH, physiology
Breast: DE, drug effects
Breast: PA, pathology
Carcinoma, Squamous Cell: PA, pathology
Cell Survival
*Cell Transformation, Neoplastic
Cell Transformation, Neoplastic: CI, chemically induced
Cell Transformation, Neoplastic: GE, genetics
Cell Transformation, Viral
Cells, Cultured
***Epithelium: PA, pathology**
Keratin: ME, metabolism
Methods
Oncogene Proteins, Viral: PH, physiology
Oncogenes
Organ Specificity
Phenotype
Polyomavirus macacae: PH, physiology
Pregnancy
Skin: ME, metabolism

L26 ANSWER 15 OF 15 MEDLINE
AN 86179852 MEDLINE

DN 86179852
TI Neoplastic conversion of human keratinocytes by adenovirus 12-SV40 virus and chemical carcinogens.
AU Rhim J S; Fujita J; Arnstein P; Aaronson S A
SO SCIENCE, (1986 Apr 18) 232 (4748) 385-8.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198607
AB Efforts to investigate the progression of events that lead human cells of epithelial origin to become neoplastic in response to carcinogenic agents have been aided by the development of tissue culture systems for propagation of epithelial cells. In the present study, nontumorigenic human epidermal keratinocytes **immortalized** by adenovirus 12 and simian virus 40 (Ad 12-SV40) were transformed by treatment with the chemical carcinogens N-methyl-N'-nitro-N-nitrosoguanidine or 4-nitroquinoline-1-oxide. Such transformants showed morphological alterations and induced carcinomas when transplanted into nude mice, whereas primary human epidermal keratinocytes treated with these chemical carcinogens failed to show any evidence of transformation. This in vitro system may be useful in assessing environmental carcinogens for human epithelial cells and in detecting new human oncogenes.
CT Check Tags: Animal; Human
*Adenoviruses, Human: ME, metabolism
Cell Line
*Cell Transformation, Neoplastic: CI, chemically induced
Cell Transformation, Neoplastic: ME, metabolism
Cell Transformation, Viral
***Epidermis: CY, cytology**
*Keratin
*Methylnitronitrosoguanidine: PD, pharmacology
Mice
Mice, Nude
Neoplasm Transplantation
*Nitroquinolines: PD, pharmacology
Oncogenes
***Polyomavirus macacae: ME, metabolism**
Skin Neoplasms: CI, chemically induced
*Skin Neoplasms: ET, etiology
Skin Neoplasms: MI, microbiology
*4-Nitroquinoline-1-oxide: PD, pharmacology

L27 ANSWER 1 OF 14 MEDLINE
AN 97301324 MEDLINE
DN 97301324
TI Growth requirements and neoplastic transformation of two types of normal human breast epithelial cells derived from reduction mammoplasty.
AU Kao C Y; Oakley C S; Welsch C W; Chang C C
CS Department of Pediatrics/Human Development, College of Human Medicine, Michigan State University, East Lansing 48824, USA.
NC CA 50430 (NCI)
CA 21104 (NCI)

ES07256 (NIEHS)
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY. ANIMAL, (1997 Apr) 33 (4) 282-8.
Journal code: BZE. ISSN: 1071-2690.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
EW 19970902

AB A chemically defined culture medium was developed to support the growth of two distinctly different types of normal human breast epithelial cells (HBEC) derived from reduction mammoplasty. Type I cells expressed luminal epithelial cell markers and were deficient in gap junctional intercellular communication (GJIC), whereas Type II cells expressed basal epithelial cell markers and were efficient in GJIC. In this study, we examined and compared the growth factor and hormone requirements of these two types of cells and a series of cell lines that were obtained by sequential transfection with SV40 DNA (extended lifespan, nontumorigenic), treatment with 5-bromodeoxyuridine (BrdU)/black light (immortal and weakly tumorigenic), and infection of a virus carrying the neu oncogene (highly tumorigenic). Growth of Type I cells was inhibited by withdrawing epidermal growth factor (EGF), hydrocortisone (HC), or insulin (INS) from the culture media, but was enhanced by fetal bovine serum (FBS) supplementation. Growth of Type II cells was inhibited by withdrawal of EGF, HC, or INS from the media, and was inhibited by FBS supplementation. Withdrawal of human transferrin (HT) or 17 beta-estradiol (E2) from the media did not alter the growth of Type I or Type II cells. SV40 transfected Type I cell lines still required EGF, HC, or INS for optimal growth. However, the highly tumorigenic cell line did not show a growth dependence on EGF, HC, or INS but did appear to require HT and 3,3',5-triiodo-D.L. thyronine (T3) for optimal growth. In addition, FBS stimulated the growth of these cell lines. Thus, this study shows that Type I HBEC are distinctly different from Type II HBEC in growth response to FBS and that neoplastically transformed Type I cells could become growth factor and hormone independent.

CT Check Tags: Animal; Female; Human; Support, U.S. Gov't, P.H.S.
Adult
*Breast: CY, cytology
Bromodeoxyuridine: PD, pharmacology
Cell Division
Cell Line, Transformed
***Cell Transformation, Neoplastic**
Culture Media
Epithelium: CY, cytology
Genes, erbB-2: PH, physiology
Growth Substances: PD, pharmacology
Hormones: PD, pharmacology
Mammaplasty
Mice
Mice, Nude
Neoplasms, Experimental
Polyomavirus macacae
Radiation-Sensitizing Agents: PD, pharmacology
Ultraviolet Rays

L27 ANSWER 2 OF 14 MEDLINE
AN 96323320 MEDLINE
DN 96323320
TI Spontaneous de-differentiation correlates with extended lifespan in transformed thyroid epithelial cells: an epigenetic mechanism of tumour progression?.
AU Bond J A; Oddweig Ness G; Rowson J; Ivan M; White D; Wynford-Thomas D
CS Cancer Research Campaign Thyroid Tumour Biology Research Group, Department of Pathology, University of Wales College of Medicine, Cardiff, UK.
SO INTERNATIONAL JOURNAL OF CANCER, (1996 Aug 7) 67 (4) 563-72. Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199611
AB Normal thyroid follicular cells, like many highly differentiated epithelia, have limited proliferative capacity. We previously showed that this could be extended by expression of the SV40 large T oncogene, but that immortal lines always lost thyroid-specific differentiation. Detailed analysis now show that clones expressing T undergo 2 mutually exclusive fates. They either (i) remain well-differentiated, in which case they undergo irreversible growth arrest after 5 to 15 p.d., or (ii) spontaneously develop poorly differentiated sub-clones that exhibit greatly extended proliferative life spans (up to 75 p.d.). The frequency of this event (> 3 per 10(4) cell divisions) greatly exceeds that expected from somatic mutation, suggesting an epigenetic basis. This is supported by our finding of rare de-differentiated epithelial cells in normal thyroid that all generate clones with extended life spans, indistinguishable from the above, following introduction of SV40 T. Escape from early mortality in differentiated thyroid epithelium therefore requires not only loss of tumour suppressor gene function (induced here by SV40 T), but also a switch in differentiation programme, with the latter effectively converting the follicular cell into a cell type with increased intrinsic proliferative potential. The analogy between this in vitro model and the progression of thyroid cancer from the well-differentiated to the highly aggressive, anaplastic form suggests that de-differentiation may play a causal rather than a passive role in this critical switch in tumour behaviour.
CT Check Tags: Human; Support, Non-U.S. Gov't
Antigens, Viral, Tumor: BI, biosynthesis
Cell Differentiation
Cell Division
Cell Line
Cell Survival
***Cell Transformation, Neoplastic**
Cells, Cultured
Clone Cells

Epithelium: CY, cytology
Oncogenes
***Polyomavirus macacae: GE, genetics**
*Thyroid Gland: CY, cytology
*Thyroid Neoplasms: PA, pathology
Time Factors
Tumor Cells, Cultured

L27 ANSWER 3 OF 14 MEDLINE
AN 96094764 MEDLINE
DN 96094764
TI Conditional transformation of mouse liver epithelial cells. An in vitro model for analysis of genetic events in hepatocarcinogenesis.
AU Lee G H; Ogawa K; Drinkwater N R
CS McArdle Laboratory for Cancer Research University of Wisconsin Medical School, Madison.
NC CA22484 (NCI)
CA07175 (NCI)
SO AMERICAN JOURNAL OF PATHOLOGY, (1995 Dec) 147 (6) 1811-22.
Journal code: 3RS. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199603
AB Primary rodent and human hepatocytes have a very limited lifespan in culture and are not readily applicable to transformation studies in vitro.

To facilitate the investigation of early genetic events involved in hepatocarcinogenesis, we examined a transformation assay system utilizing conditionally immortalized mouse liver epithelial cells as an alternative to primary hepatocytes. By infecting primary mouse hepatocytes with a recombinant retrovirus carrying a temperature-sensitive simian virus 40 large T antigen gene, two mouse liver epithelial cell lines, CHST8 and CHST10-2.1, were established. Because of the heat-labile nature of the large T antigen, the cell lines proliferated rapidly at 33 degrees C, but were growth-arrested at 39 degrees C. Because activated c-H-ras and c-myc oncogenes are frequently found to be involved in mouse hepatocarcinogenesis in vivo, we assessed whether those oncogenes can complement the immortalizing function of the large T antigen at the nonpermissive temperature. When CHST8 cells were doubly transfected with activated c-H-ras and c-myc at 33 degrees C, they exhibited clonal growth ability even after shifting the temperature to 39 degrees C. However, neither c-H-ras nor c-myc alone allowed growth at 39 degrees C. On the other hand, c-H-ras alone was sufficient for overcoming the growth defect of CHST10-2.1 cells at 39 degrees C, whereas c-myc alone was again ineffective. Northern blot studies revealed that endogenous c-myc expression was significantly downregulated in the parental CHST8 cells after a temperature shift from 33 to 39 degrees C. In contrast, in the parental CHST10-2.1 cells, appreciable c-myc expression was observed at both temperatures. These results indicate that c-H-ras and c-myc can cooperate in complementing the ability of the temperature-sensitive large T antigen to immortalize mouse liver cells at the nonpermissive temperature. In addition, the mutant c-H-ras, but not c-myc, cooperated with the functional T antigen at 33 degrees C to allow growth in soft agarose of the CHST8 and CHST10-2.1 cell lines. However, cell lines carrying mutant c-H-ras and overexpressing c-myc were unable to grow in

soft agarose at 39 degrees C. Thus, the two cellular oncogenes were insufficient for full transformation of the liver epithelial cells. The present in vitro model should be useful for investigating molecular events involved in both early and late stages of hepatocarcinogenesis.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antigens, Polyomavirus Transforming: GE, genetics
Base Sequence
Cell Transformation, Neoplastic: GE, genetics
***Cell Transformation, Neoplastic: PA, pathology**
Cells, Cultured
Epithelium: PA, pathology
Genes, myc: GE, genetics
Genes, ras: GE, genetics
Genetic Vectors: GE, genetics
Liver: CY, cytology
*Liver: PA, pathology
Mice
Models, Biological
Molecular Sequence Data
Mutagenesis
Polymerase Chain Reaction
Polyomavirus macacae: GE, genetics
Retroviridae: GE, genetics

L27 ANSWER 4 OF 14 MEDLINE
AN 94334033 MEDLINE
DN 94334033
TI Characterization of intraocular tumors arising in transgenic mice.
AU Anand R; Ma D; Alizadeh H; Comerford S A; Sambrook J F; Gething M J; McLean I W; Niederkorn J Y
CS Department of Ophthalmology, University of Texas Southwestern Medical Center, Dallas 75235..
NC CA30276 (NCI)
HLA5944
SO INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Aug) 35 (9) 3533-9.
Journal code: GWI. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199411
AB PURPOSE. To characterize intraocular tumors that arise by in situ transformation in the choroid-retinal pigment epithelium (RPE) in transgenic mice bearing the SV40 oncogene under the control of the mouse tyrosinase promoter. METHODS. Tumors from TySV40 transgenic mice were characterized in vivo and in vitro by immunohistology, compound microscopy, and electron microscopy. Tumor cell lines were established and characterized for growth and metastatic potential in the eyes of nude mice. RESULTS. On light microscopy, ocular tumors were predominantly epithelioid, although occasional clusters of spindle cells were also present. Transmission electron microscopy revealed the presence of numerous basal infoldings and abundant multilaminated basement membranes on the ocular tumors. Tumors stained with antibodies to melanoma-associated antigens, gangliosides GD2 and GD3, and the SV40 T antigen. Radiolabeled transgenic tumor cells preferentially localized in

the liver after intravenous injection in normal mice. Intracamerally transplanted transgenic tumors metastasized from the eyes to the livers of nude mice. CONCLUSIONS. In TySV40 transgenic mice, intraocular tumors develop that arise at the choroid-RPE interface, and they display morphologic and ultrastructural features consistent with RPE carcinomas. However, the transgenic tumors express melanoma-associated antigens and a propensity to metastasize to the liver, two features characteristic of uveal melanomas. The TySV40 transgenic murine tumors represent potentially useful tools for investigations into the biology and metastasis of intraocular neoplasms.

CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antigens, Neoplasm: AN, analysis
*Carcinoma: SC, secondary
Cell Transformation, Neoplastic
*Choroid Neoplasms: PA, pathology
Fluorescent Antibody Technique
Liver Neoplasms: SC, secondary
Mice
Mice, Nude
Mice, Transgenic
Oncogenes: GE, genetics
***Pigment Epithelium of Eye: UL, ultrastructure**
Polyomavirus macacae: GE, genetics
*Retinal Diseases: PA, pathology

L27 ANSWER 5 OF 14 MEDLINE
AN 93238843 MEDLINE
DN 93238843
TI Oncogene-mediated propagation of tracheal epithelial cells from two cystic fibrosis fetuses with different mutations. Characterization of CFT-1 and CFT-2 cells in culture.
AU Lemnaouar M; Chastre E; Paul A; Mergey M; Veissi`ere D; Cherqui G; Barbry P; Simon-Bouy B; Fanen P; Gespach C; et al
CS Inserm U. 181, Faculte de Medecine Saint-Antoine, Paris, France..
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, (1993 Mar) 23 (3) 151-60. Journal code: EN3. ISSN: 0014-2972.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199307
AB Primary tracheal epithelial cells obtained from two fetusés with cystic fibrosis (CF) were successfully transfected with a plasmid vector recombined with the large T oncogene of SV40. The resulting tracheal cells were propagated in culture for up to 25 passages and retained the mutations of the CF genes carried by the two fetuses, one heterozygous for the S549N and N1303K substitutions (CFT-1 cells), and the other homozygous for the most common deletion delta F508 (CFT-2 cells). The transfected cells: (a) expressed the SV40 large T oncogene, as determined by immunofluorescence and Northern blot analysis; (b) retained typical

epithelial morphology, as assessed by the presence of microvilli, desmosomes, gap junctions, and cytokeratin expression; (c) were fully responsive to the cAMP-stimulating agents isoproterenol, forskolin and vasoactive intestinal peptide for cAMP production and PKA activation; (d) do not produce any tumour in the athymic nude mice; (e) were diploid and tetraploid with a normal chromosomal complement at early passages, and (f) exhibited the abnormal regulation of chloride conductance characteristic of CF. These results indicate that CFT-1 and CFT-2 cells constitute a suitable model for: (a) comparison of the maturation and function of the CFTR protein mutated in the two nucleotide-binding domains; (2) analysis of the biochemical defect in CF epithelial airway cells, (c) development of new therapeutic agents, and correction of the CF defect by gene replacement therapy in vitro.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't
Cell Transformation, Neoplastic
Cells, Cultured
*Cystic Fibrosis: GE, genetics
*Cystic Fibrosis: PA, pathology
Epithelium: PA, pathology
Fetus: PA, pathology
Gene Expression
*Membrane Proteins: GE, genetics
Mice
Mice, Nude
Mutation
***Oncogenes**
Polyomavirus macacae: GE, genetics
Trachea: PA, pathology
Transfection

L27 ANSWER 6 OF 14 MEDLINE
AN 93086715 MEDLINE
DN 93086715
TI A new approach to the molecular basis of neoplastic transformation in the brain.
AU Wiestler O D; Brustle O; Eibl R H; Radner H; Von Deimling A; Plate K; Aguzzi A; Kleihues P
CS Institute of Neuropathology, University of Zurich, Switzerland.
SO NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY, (1992 Oct) 18 (5) 443-53. Journal code: NY0. ISSN: 0305-1846.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
AB Gene transfer into living organisms has evolved as a powerful approach to study in vivo effects of specific genes and to devise animal models of hereditary disorders. We have been particularly interested in an approach to introducing transforming genes into the nervous system. Since specific promoter sequences for targeting the expression of a transgene to many cell types of the brain are not yet isolated, a suitable transgenic mouse model was not available for these experiments. This has prompted us to develop an alternative strategy for gene transfer into the brain. The rationale is to introduce foreign genes into fetal brain transplants using embryonic CNS as donor tissue and replication-defective retroviral vectors

as genetic vehicles. This technique relies on the extraordinary organotypic differentiation capacity of neural grafts and the expression of retrovirally transmitted genes in different cell types of CNS transplants. In contrast to transgenic animals but analogous to sporadic tumour formation, target cells for the retroviral vector will develop in an environment of unmodified neural tissue. We have introduced a number of neurotropic oncogenes into fetal brain transplants to study potential effects of such genes on the brain. This review will summarize some of the findings which have emerged from this experimental study including the tropism of several genes for endothelial cells, attempts to identify cooperating combinations of transforming genes and an experimental model for primitive neuroectodermal tumours in neural grafts.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Brain Tissue Transplantation
***Cell Transformation, Neoplastic**
Endothelium, Vascular: CY, cytology
Endothelium, Vascular: PH, physiology
Fetal Tissue Transplantation
Genes, Viral
Nervous System Neoplasms: GE, genetics
***Oncogenes**
Phenotype
Polyomavirus macacae: GE, genetics
*Retroviridae: GE, genetics
*Transfection

L27 ANSWER 7 OF 14 MEDLINE
AN 92363641 MEDLINE
DN 92363641
TI Single-steep transformation of human breast epithelial cells by SV40 large T oncogene.
AU Berthon P; Goubin G; Dutrillaux B; Degeorges A; Faille A; Gespach C; Calvo F
CS Laboratoire de Pharmacologie, Hopital Saint-Louis, Paris, France..
SO INTERNATIONAL JOURNAL OF CANCER, (1992 Aug 19) 52 (1) 92-7.
Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199211
AB Normal human mammary epithelial cell (HMEC) cultures originating from 2 mammoplasty reduction surgical samples were transfected with replication-defective SV 40 DNA. Two independent cell lines designated as S2T2 and S1T3, selected for their increased proliferation potential and lifespan, were propagated for greater than 22 months in culture. They maintained a near-diploid karyotype with few chromosomal markers such as trisomy 1q (S1T3) and trisomy 8q (S2T2), which are most common in breast cancer in vivo. Immortalized S1T3 cells were not tumorigenic, whereas S2T2 cells produced slowly growing tumors in nude mice. One tumor was propagated in vitro and the transformed NS2T2 cell line subsequently raised 100% large tumors in the nude mouse. Rearrangement of the SV40

genome was observed in NS2T2 cells, which was not associated with increased expression of large T antigen. S1T3, S2T2 and transformed NS2T2 cell lines expressed cytokeratins CK18, CK19, the mammary-specific antigen DF3, and functional EGF receptors. Single-step immortalization and malignant transformation of human breast epithelial cells can thus occur upon transfection with SV40 large T oncogene. The chromosomal abnormalities observed in these cell lines suggest that they could offer a model for the study of breast-tumor progression in vitro.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Adult
*Breast: PA, pathology
Cell Division
***Cell Transformation, Neoplastic**
Chromosome Aberrations
DNA, Viral: AN, analysis
Epithelium: PA, pathology
***Oncogenes**
***Polyomavirus macacae: GE, genetics**
Transfection

L27 ANSWER 8 OF 14 MEDLINE
AN 92257441 MEDLINE
DN 92257441
TI Chromosome losses in tumorigenic revertants of EJ/ras-expressing somatic cell hybrids.
AU Pratt C I; Wu S Q; Bhattacharya M; Kao C; Gilchrist K W; Reznikoff C A
CS Cellular and Molecular Biology Program, University of Wisconsin Clinical Cancer Center, Madison 53792.
NC NCI-R01-CA29525-12 (NCI)
P01-BM144-CA13-1 (NCI)
5 T32 GM07215 (NIGMS)
+
SO CANCER GENETICS AND CYTOGENETICS, (1992 Apr) 59 (2) 180-90.
Journal code: CMT. ISSN: 0165-4608.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199208
AB Tumorigenic transformation of SV40-immortalized human uroepithelial cells (SV-HUC) after transfection with EJ/ras was previously reported to be a rare event. To test the hypothesis that ras transformation requires loss of suppressor genes, somatic cell hybrids were generated between a rare tumorigenic transformant and an isogeneic nontumorigenic EJ/ras transfectant obtained in the same experiment. Both parental cell lines, as well as all hybrid progeny, expressed mutant p21 ras protein, but injections of three such independent hybrids into athymic nude mice at passage (P) 4 demonstrated that tumorigenicity was suppressed at 20 of 22 sites. Two tumors developed, after a relatively long 17-week latent period, as compared with a 4-week latent period for the tumorigenic parent. All three hybrids produced tumors at P8, but these showed different latent periods (3-14 weeks). Revertant hybrid tumors were high-grade carcinomas. Cell lines derived from these tumors expressed mutant p21 ras and retained at least 1 EJ/ras integration site.

analysis of six independent hybrid tumor revertants showed that each had a unique clonal karyotype. Losses of two or more homologues of 1p, 3p, 4, 8, 10p, 11p, 13q, and 18 were identified in one or more tumorigenic revertants. Losses of all these chromosomes were previously associated with transformation of SV-HUC by EJ/ras, but were also associated with chemical transformation of SV-HUC in tumors that did not express mutant ras. Genetic losses involving most of these chromosomes have also been identified in clinical bladder cancers (i.e., 1p, 3p, 8, 11p, 13 and 18q).

These data show that expression of EJ/ras does not negate or significantly alter requirements for multiple genetic losses in HUC tumorigenesis.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Bladder: CY, cytology
*Bladder Neoplasms: GE, genetics
*Carcinoma: GE, genetics
Cell Line, Transformed
***Cell Transformation, Neoplastic: GE, genetics**
*Chromosome Deletion
*Chromosomes, Human
Chromosomes, Human, Pair 1
Chromosomes, Human, Pair 11
Chromosomes, Human, Pair 13
Chromosomes, Human, Pair 18
Chromosomes, Human, Pair 3
Chromosomes, Human, Pair 8
Epithelium: CY, cytology
Gene Expression Regulation, Neoplastic
***Genes, ras**
Genes, Suppressor
Hybrid Cells
Mice
Mice, Nude
Polyomavirus macacae
Proto-Oncogene Protein p21(ras): AN, analysis
Transfection

L27 ANSWER 9 OF 14 MEDLINE
AN 92119630 MEDLINE
DN 92119630
TI Neoplastic progression by EJ/ras at different steps of transformation in vitro of human uroepithelial cells.
AU Pratt C I; Kao C H; Wu S Q; Gilchrist K W; Oyasu R; Reznikoff C A
CS Cellular and Molecular Biology Program, University of Wisconsin, Madison 53792.
NC R01-CA29525-12 (NCI)
P01-BM144-CA13-1 (NCI)
5 T32 GM07215 (NIGMS)
SO CANCER RESEARCH, (1992 Feb 1) 52 (3) 688-95.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals

EM 199204
AB The biological effects of expression of mutant ras at different stages of human uroepithelial cell (HUC) tumorigenesis were tested after transfection of EJ/ras into nonestablished HUC and three isogeneic cell lines representing different steps in HUC transformation in vitro. Transfection with EJ/ras failed to immortalize diploid HUC and also failed to cause tumorigenic conversion of a near-diploid SV40-immortalized HUC line (SV-HUC) except at one of six nude mouse inoculation sites. In contrast, EJ/ras-transfected aneuploid low-grade squamous cell carcinoma cells formed undifferentiated, invasive carcinomas at four of six inoculation sites. Furthermore, EJ/ras accelerated tumor growth in MC-ppT11-HA2, an aneuploid high-grade transitional cell carcinoma line, as determined by decreased tumor latent periods and doubling times. These results suggest that EJ/ras contributes to progression, possibly by accelerating tumor growth, but does not in itself cause tumorigenic transformation of uroepithelial cells. To test whether chromosome losses accompanied EJ/ras transformation of SV-HUC, the karyotype of the one SV-HUC tumorigenic transformant obtained (above) was examined. This tumor cell line showed losses of chromosome arms 3p, 10p, 11p, and 18, all of which have been hypothesized to contain genes that suppress cancer development. Therefore, these results also provide new evidence suggesting that genetic losses may be required for mutant ras to contribute to HUC tumorigenic progression.
CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Bladder: CY, cytology
Bladder: PA, pathology
*Bladder Neoplasms: GE, genetics
Bladder Neoplasms: PA, pathology
Cell Division
Cell Line, Transformed
***Cell Transformation, Neoplastic**
Cells, Cultured
Chromosome Banding
Epithelium: CY, cytology
***Genes, ras**
Karyotyping
Mice
Mice, Nude
Mitosis
*Mutation
Neoplasm Invasiveness
Neoplasm Transplantation
Polyomavirus macacae: GE, genetics
Proto-Oncogene Protein p21(ras): AN, analysis
Proto-Oncogene Protein p21(ras): BI, biosynthesis
Proto-Oncogene Protein p21(ras): GE, genetics
*Transfection
3T3 Cells

L27 ANSWER 10 OF 14 MEDLINE
AN 91301846 MEDLINE
DN 91301846
TI A human bronchial epithelial cell strain with unusual in vitro growth

potential which undergoes neoplastic transformation after SV40 T antigen gene transfection.

AU Reddel R R; Hsu I C; Mass M J; Hukku B; Gerwin B I; Salghetti S E; Somers A N; Galati A J; Gunning WT I I I; Harris C C; et al
CS Laboratory of Human Carcinogenesis, National Cancer Institute, Bethesda, MD 20892..

NC N01-CP-21017 (NCI)
CA28950 (NCI)
SO INTERNATIONAL JOURNAL OF CANCER, (1991 Jul 9) 48 (5) 764-73.
Journal code: GQU. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199110

AB Bronchial epithelial cells were cultured from an individual with no evidence of malignant disease. These cells, designated HB56B, had a greatly extended in vitro life-span, being able to undergo 50 passages and 200 population doublings in contrast to the usual 3 to 4 passages and 20 to 30 population doublings characteristic of normal human bronchial epithelial cells. HB56B cells had karyotypic evidence of an amplified region on the short arm of chromosome II. Unlike normal bronchial epithelial cells, which undergo terminal squamous differentiation in vitro in response to fetal bovine serum, HB56B cells were only minimally affected by serum. These cells were readily established as an immortalized cell line, HB56B/5T, following transfection with a plasmid containing SV40 early region DNA. HB56B cells were non-tumorigenic in athymic nude mice, but HB56B/5T cells within a few passages of transfection with the SV40 plasmid formed tumors of which 28/37 regressed. HB56B cells may offer an experimental system for the study of proliferation, differentiation, and senescence control in human bronchial epithelial cells.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Adult
*Antigens, Polyomavirus Transforming: GE, genetics
*Bronchi: CY, cytology
*Cell Division
Cell Line
***Cell Transformation, Neoplastic**
Chromosome Abnormalities
Chromosomes, Human, Pair 11
DNA, Neoplasm: IP, isolation & purification
Epithelium: CY, cytology
Isoenzymes: AN, analysis
Isoenzymes: GE, genetics
Karyotyping
Keratin: AN, analysis
Mice
Mice, Nude
Neoplasm Transplantation
Oncogenes
***Polyomavirus macacae: GE, genetics**
Tissue Culture: MT, methods

*Transfection
Transplantation, Heterologous

L27 ANSWER 11 OF 14 MEDLINE
AN 90315652 MEDLINE
DN 90315652
TI EJ/ras neoplastic transformation of simian virus 40-immortalized human uroepithelial cells: a rare event.
AU Christian B J; Kao C H; Wu S Q; Meisner L F; Reznikoff C A
CS Department of Human Oncology, University of Wisconsin Clinical Cancer Center, Madison 53792.
NC 5-T32-CA 09474-03 (NCI)
CA-29525-08 (NCI)
SO CANCER RESEARCH, (1990 Aug 1) 50 (15) 4779-86.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199010
AB To determine if expression of mutant p21 ras could convert Simian Virus 40-immortalized human uroepithelial cell line (SV-HUC) to tumorigenicity, SV-HUC cells were transfected with pSV2-neo (a neomycin-resistant gene) or PREJ/ras (c-HA-ras-1 with the 12th codon mutation and neo). Seven independent G418-resistant clones (A----G) were isolated from each group (SV-HUC/ras and SV-HUC/neo). SV-HUC/ras clones were morphologically altered, while SV-HUC/neo clones retained a typical SV-HUC epithelial morphology. Electrophoretic analysis of immunoprecipitated ras proteins detected altered p21 ras protein in four of seven SV-HUC/ras clones at passage (P)2 and in five of seven clones at P12 posttransfection. The relative levels of ras p21 differed among the clones and appeared to increase with passage in culture. RNA and DNA dot blot analyses showed that clones with more abundant mutant p21 also had higher ras RNA levels and, in one case, increased ras gene copy number. No altered ras protein was detected in any SV-HUC/neo clones. ras- and neo-transfected clones were tested for tumorigenicity at P2 posttransfection and again at P12 by four s.c. inoculations each into athymic nude mice. None of 56 inoculations of SV-HUC/neo clones was tumorigenic. None of the SV-HUC/ras clones at P2 gave rise to tumors at all four injection sites. However, two ras-transfected clones, SV-HUC/ras-B and SV-HUC/ras-F, produced one tumor each. One clone, SV-HUC/ras-D which produced abundant mutant p21, was negative when inoculated at P2, but produced tumors in four of four sites when reinoculated after ten passages in vitro. All tumorigenic clones had detectable levels of mutant ras p21. However, the relative levels of altered p21 ras protein among the SV-HUC/ras clones did not directly predict their tumorigenic potential, as several nontumorigenic SV-HUC/ras clones had protein levels equal to or higher than the most tumorigenic clone (SV-HUC/ras-D at P12). Cell lines established from the tumor explants exhibited higher ras gene copy numbers, higher RNA levels, and more abundant p21 than was seen in the clones at the time of inoculation. Therefore, increases in ras protein abundance occurred during tumor formation in vivo, as well as during passage of cells in culture, and such cells apparently had a selective growth advantage. However, expression of abundant mutant ras protein was not in itself sufficient for neoplastic

transformation of SV-HUC.(ABSTRACT TRUNCATED AT 400 WORDS)
CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Bladder
Cell Line
***Cell Transformation, Neoplastic**
Clone Cells
Epithelium
***Genes, ras**
Mice
Mice, Nude
Neoplasm Transplantation
Oncogene Protein p21(ras): IP, isolation & purification
Plasmids
***Polyomavirus macacae: GE, genetics**
*Transfection
Transplantation, Heterologous

L27 ANSWER 12 OF 14 MEDLINE
AN 90099299 MEDLINE
DN 90099299
TI Cooperation of c-raf-1 and c-myc protooncogenes in the neoplastic transformation of simian virus 40 large tumor antigen-immortalized human bronchial epithelial cells.
AU Pfeifer A M; Mark G E 3d; Malan-Shibley L; Graziano S; Amstad P; Harris C C
CS Laboratory of Human Carcinogenesis, National Cancer Institute, Bethesda, MD 20892.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 Dec) 86 (24) 10075-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199004
AB Overexpression of c-raf-1 and the myc family of protooncogenes is primarily associated with small cell carcinoma, which accounts for approximately 25% of human lung cancer. To determine the functional significance of the c-raf-1 and/or c-myc gene expression in lung carcinogenesis and to delineate the relationship between protooncogene expression and tumor phenotype, we introduced both protooncogenes, alone or in combination, into human bronchial epithelial cells. Two retroviral recombinants, pZip-raf and pZip-myc, containing the complete coding sequences of the human c-raf-1 and murine c-myc genes, respectively, were constructed and transfected into simian virus 40 large tumor antigen-immortalized bronchial epithelial cells (BEAS-2B); this was followed by selection for G418 resistance. BEAS-2B cells expressing both the transfected c-raf-1 and c-myc sequences formed large cell carcinomas in athymic nude mice with a latency of 4-21 weeks, whereas either pZip-raf- or pZip-myc-transfected cells were nontumorigenic after 12 months. Cell lines established from tumors (designated RMT) revealed the presence of the cotransfected c-raf-1 and c-myc sequences and expressed morphological, chromosomal, and isoenzyme markers, which identified BEAS-2B cells as the progenitor line of the tumors. A significant increase
in the mRNA levels of neuron-specific enolase was detected in BEAS-2B

cells containing both the c-raf-1 and c-myc genes and derived tumor cell lines. The data demonstrate that the concomitant expression of the c-raf and c-myc protooncogenes causes neoplastic transformation of human bronchial epithelial cells resulting in large cell carcinomas with certain neuroendocrine markers. The presented model system should be useful in studies of molecular events involved in multistage lung carcinogenesis.

CT Check Tags: Animal; Human
*Antigens, Polyomavirus Transforming: GE, genetics
Blotting, Southern
Bronchi
Cell Line
***Cell Transformation, Neoplastic**
Chimera
Epithelium
Gene Expression
Immunoassay
Mice
Mice, Nude
Molecular Weight
Neoplasm Transplantation
***Polyomavirus macacae: GE, genetics**
Polyomavirus macacae: IM, immunology
*Protein-Tyrosine Kinase: GE, genetics
*Proto-Oncogene Proteins: GE, genetics
Proto-Oncogene Proteins: IP, isolation & purification
***Proto-Oncogenes**
Transfection
Transplantation, Heterologous

L27 ANSWER 13 OF 14 MEDLINE
AN 89240702 MEDLINE
DN 89240702
TI Transfection of fetal rat intestinal epithelial cells by viral oncogenes: establishment and characterization of the E1A-immortalized SLC-11 cell line.
AU Emami S; Mir L; Gespach C; Rosselin G
CS Institut National de la Sante et de la Recherche Medicale Unite 55, Hopital Saint-Antoine, Paris, France..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1989 May) 86 (9) 3194-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198908
AB Intestinal epithelial cells from 19-day-old rat fetuses underwent electropermeabilization and were successfully transfected by three recombinant plasmids containing the cloned oncogenes from the human adenovirus type 2 early region E1A (SLC-11 cells) and polyoma virus and simian virus 40 large T tumor antigens (SLC-21 and SLC-41 cells). SLC-11 cells were propagated for 21 months in culture (current passage, 76; doubling time, 17 hr) and were immortalized by E1A, as shown by RNA transfer blot (Northern blot) analysis and indirect immunofluorescence of the nuclear oncoproteins. These cells were not tumorigenic in either athymic nude mice or syngeneic Wistar rats and showed a nearly normal

karyotype with minimal chromosomal changes. The immortalized epithelial cell line SLC-11 retained several of the phenotypes observed in the parent cells of the intestinal mucosa, including cytoplasmic villin, cytokeratins, enkephalinase, and cell surface receptors sensitive to vasoactive intestinal peptide. It is concluded that immortal SLC-11 cells are a suitable model for studying the proliferation and differentiation of epithelial intestinal cells and analyzing cancer progression in the gastrointestinal tract.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Adenoviridae: GE, genetics
Antigens, Polyomavirus Transforming: GE, genetics
Cell Division
Cell Line
Cell Transformation, Neoplastic
Cyclic AMP: ME, metabolism
DNA, Recombinant
Epithelium
Fetus
Fluorescent Antibody Technique
*Intestines
Intestines: UL, ultrastructure
Karyotyping
Microscopy, Electron
Nucleic Acid Hybridization
***Oncogenes**
Plasmids
Polyomavirus macacae: IM, immunology
Rats
RNA: GE, genetics
*Transfection
Vasoactive Intestinal Peptide: ME, metabolism

L27 ANSWER 14 OF 14 MEDLINE
AN 72251204 MEDLINE
DN 72251204
TI Experimental malignant tumors from retinal pigment epithelium.
AU Albert D M; Tso M O; Rabson A S
SO ARCHIVES OF OPHTHALMOLOGY, (1972 Jul) 88 (1) 70-4.
Journal code: 830. ISSN: 0003-9950.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 197212
CT Check Tags: Animal; Male
***Cell Transformation, Neoplastic**
Disease Models, Animal
Epithelium
Hamsters
Neoplasm Metastasis
*Neoplasms, Experimental
***Polyomavirus macacae**
*Retina: CY, cytology
*Retinal Pigments